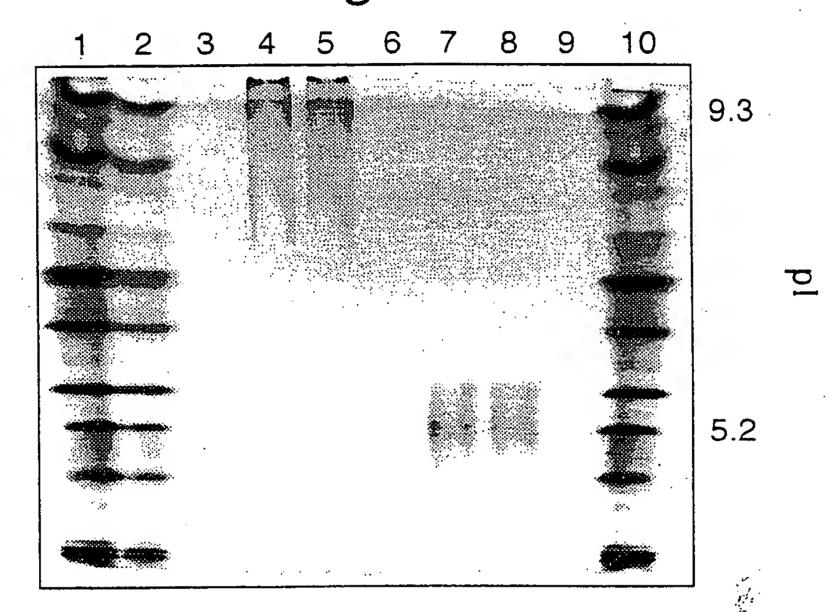
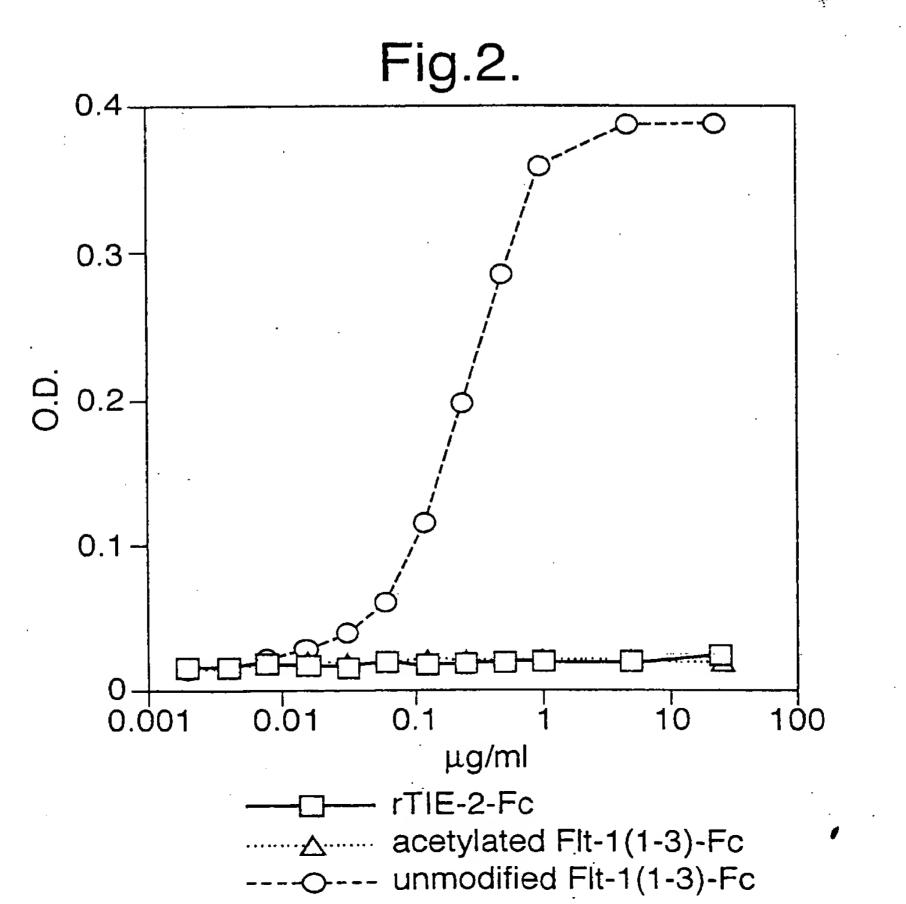
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Fig.1.

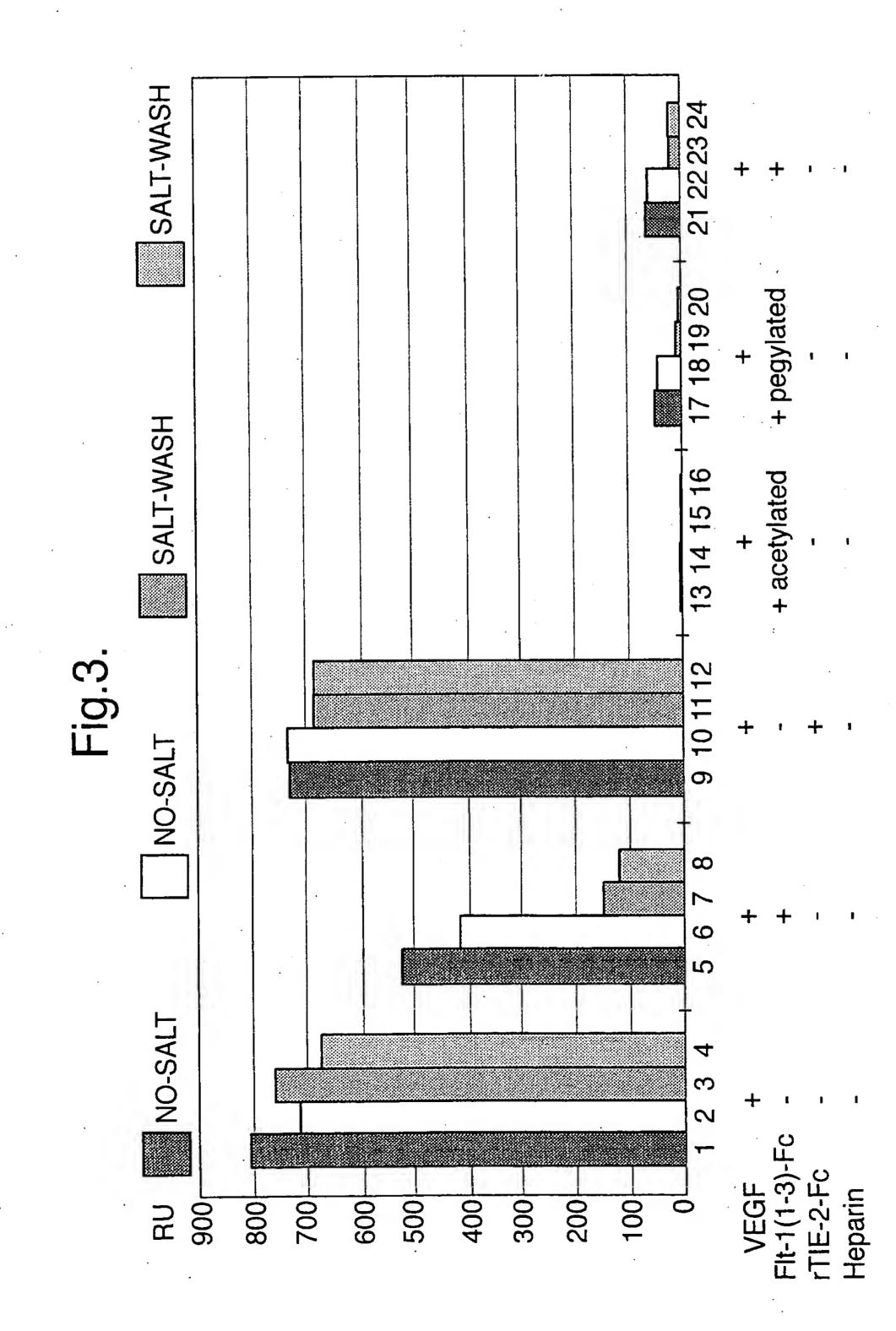




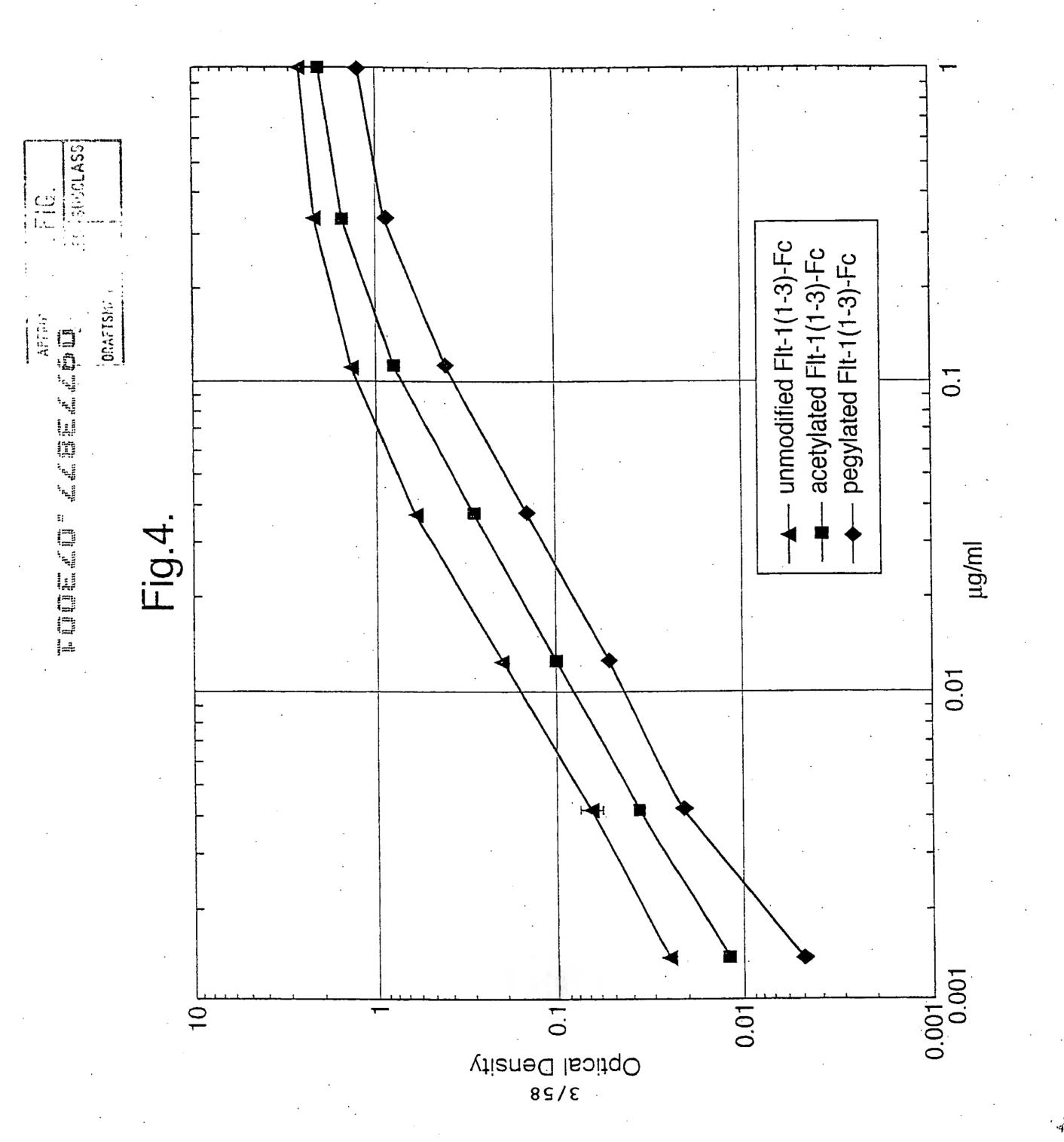
SUBCLASS

DRAFTS!..

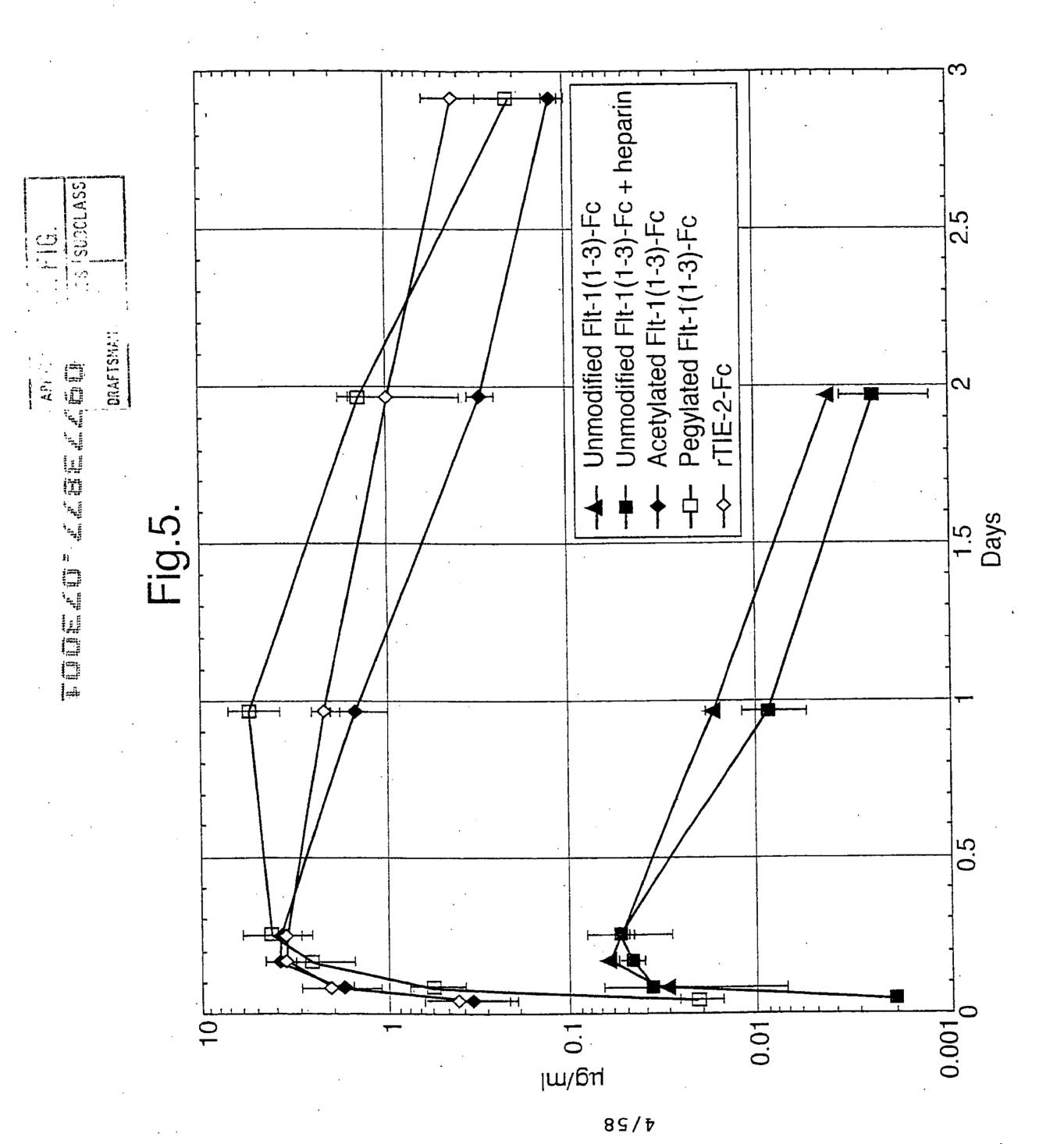




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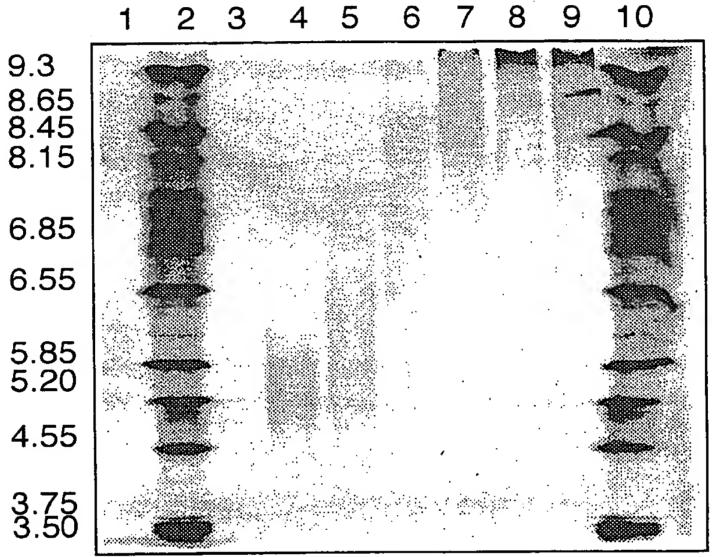


Fig.6B.

11 12 13 14 15 16 17 18 19 20

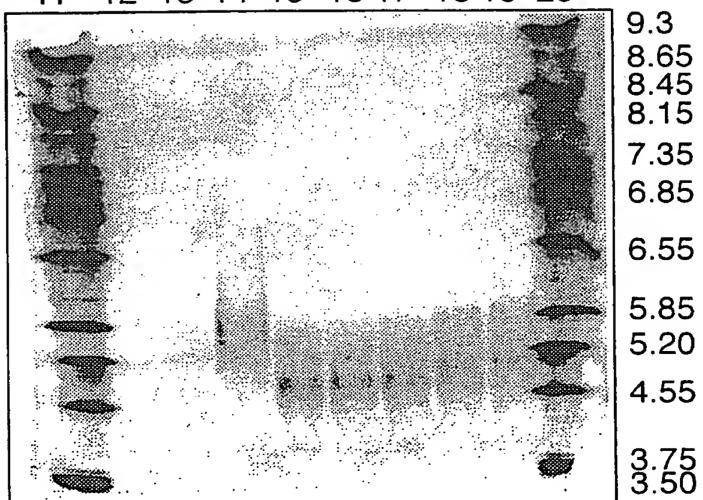
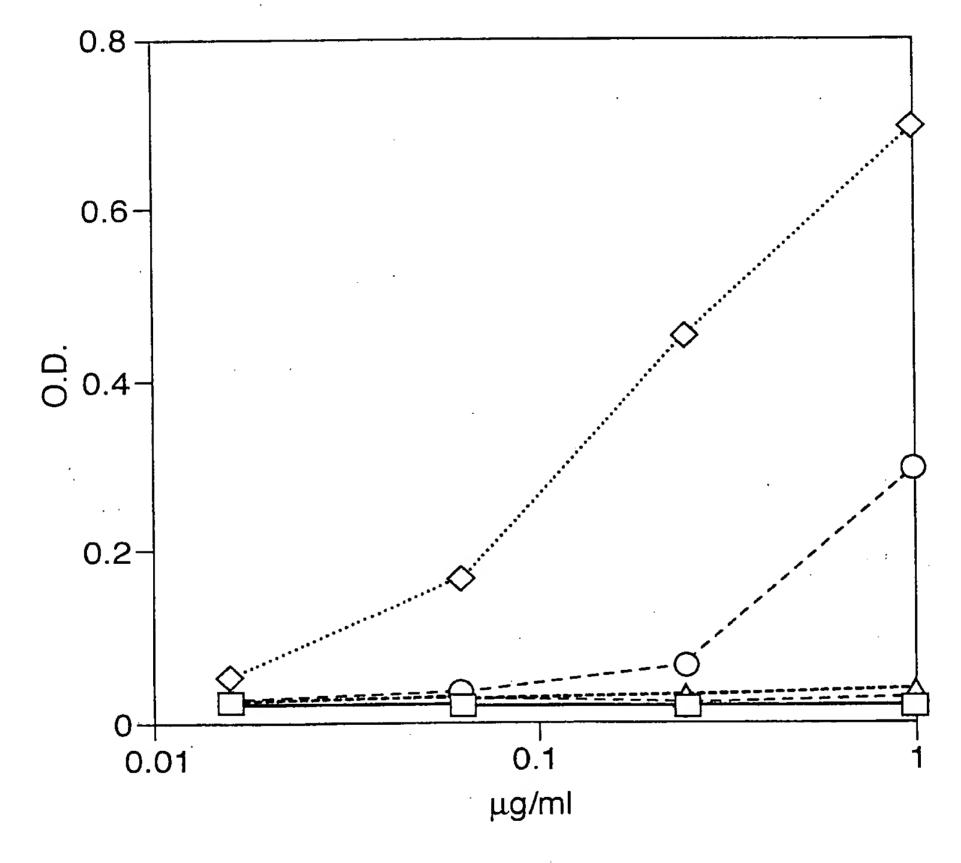


Fig.7.



rTIE-2-Fc

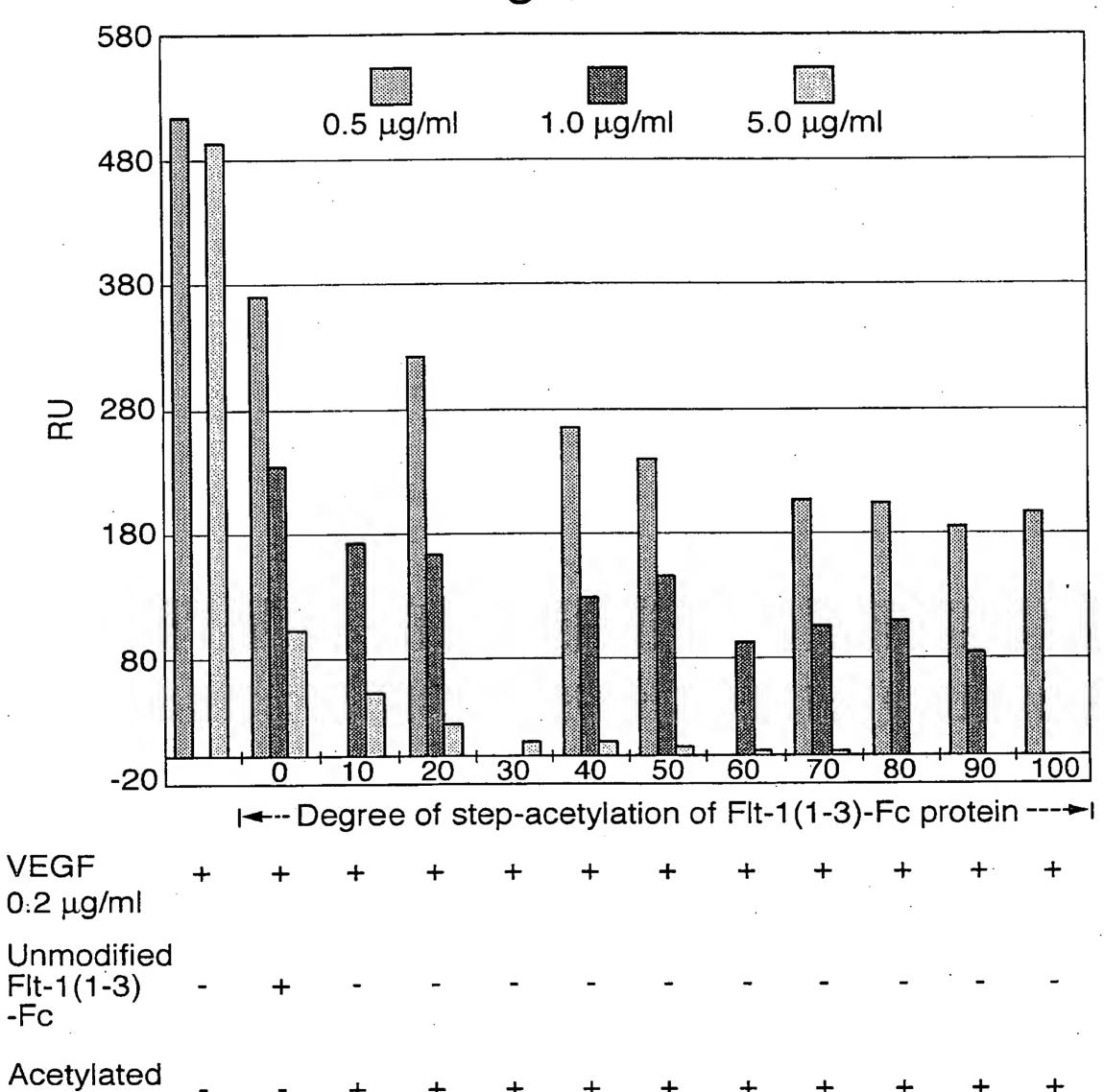
unmodified Flt-1(1-3)-Fc acetylated Flt-1(1-3)-Fc (10X)

----- acetylated Flt-1(1-3)-Fc (20X)

--- acetylated Flt-1(1-3)-Fc (30X)

> Flt-1(1-3) -Fc

Fig.8.



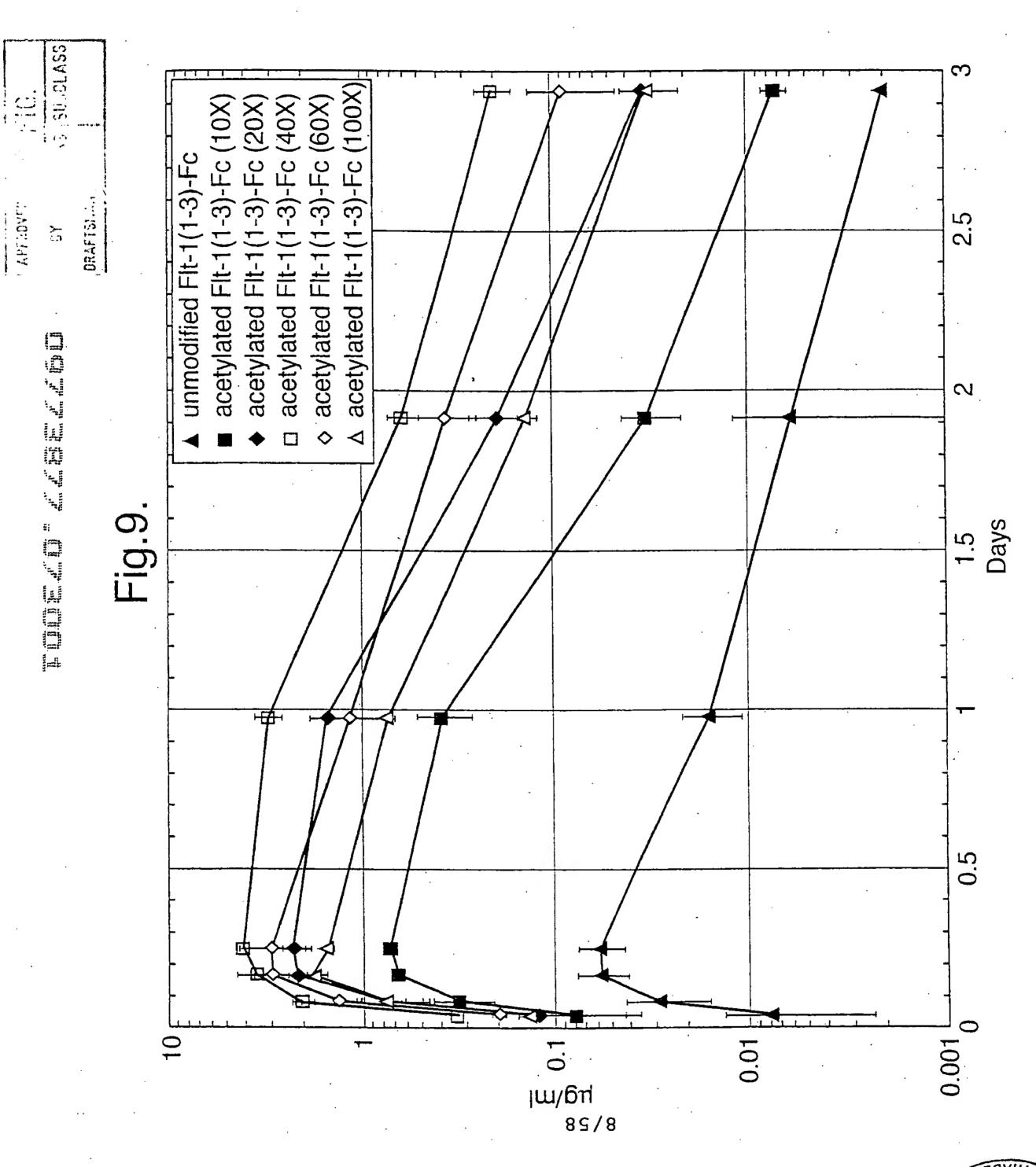






Fig.10A.

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TAC CAG TOO	ATG 1	ACC C	LC LC	G CC	cc c	AG (GAC	GAC	ACG	CGC	GAC	GAG	TCG	ACA	GAC	GAA	GAG
Met Val Ser	Tyr !	rp A	sp Th	ir Gl	ly V	al l	Leu	Leu	Cys	Ala	Leu	Leu	Ser	Cys	Leu	Leu	Leu>
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CAC ATC AT	G CAA	GCA G	GC C	AG A	CA	CTG	CAT	CTC	CAA	TGC	AGG	GGG	GAA	GCA	GCC	CAI	AAA '
GTG TAG TA	CGTT	CGT C	CCG G	TC T	GT (GAC	GTA	GAG	GTT	ACG	TCC	.ccc	CTT	CGT	CGG	GT	TTT
His Ile Me	t Gln	Ala (Gly G	ln T	hr 1	Leu	His	Leu	Gln	Cys	Arg	Gly	Glu	Ala	Ala	His	: Lys>
	190		20	0			210			2	20			230		.4.	240
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TGG TCT TT	G CCT	GAA A	ATG G	TG A	GT .	AAG	GAA	AGC	GAA	AGG	CTC	AGC	ATA	ACI	' AAA		l' GCC
ACC AGA AA	C GGA	CTT :	TAC C	AC 1	CA	TTC	CTT	TCG	CTT	TCC	GAC	Com	TAT	TOP	7 .1.1.1	· AG	A CGG ~ N] a ~
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Cys Gly Ar	g Asn	Gly	Lys C	in I	Phe	Cys	Ser	Thr	Leu	Th	r Lei	ı Asr	Thi	c Ala	a Gl	n Al	a Asn>
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GTG TGA C	CG AAG	ATG	TCG 1	ACG '	TTT	ATA	GAT	CGA	CA	r GG	A TG	A AG	r TT	C TT	C TT	C C1	T TGT
His Thr G	ly Phe	Tyr	Ser (Cys :	Lys	Tyr	Leu	ı Ala	Va.	l Pr	o Th	r Sei	r Ly	s ry	s Ly	s Gl	u Thr>
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CTT AGA C																	
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CTT TAG G	GG CIT	AAT 1	TAT	GTG	TAC	TG	A CT	T CC	T TC	C CI	C G	G CA	G T?	A GC	G A	CG G	CC CAA
Glu Ile F	ro Glu	ı Ile	Ile	His	Met	Th	r Gl	u Gl	y Ar	g G	lu Le	eu Va	1 11	le Pi	10 C	ys A	rg Val>
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Fig. 10B.

GGA AAA CGC ATA ATC TGG GAC AGT AGA AAG GGC TTC ATC ATA TCA AAT GCA ACG TAC AAA CCT TTT GCG TAT TAG ACC CTG TCA TCT TTC CCG AAG TAG TAT AGT TTA CGT TGC ATG TTT Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys> GAA ATA GGG CTT CTG ACC TGT GAA GCA ACA GTC AAT GGG CAT TTG TAT AAG ACA AAC TAT CTT TAT CCC GAA GAC TGG ACA CTT CGT TGT CAG TTA CCC GTA AAC ATA TTC TGT TTG ATA Glu Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr> CTC ACA CAT CGA CAA ACC AAT ACA ATC ATA GAT GTC CAA ATA AGC ACA CCA CGC CCA GTC GAG TGT GTA GCT GTT TGG TTA TGT TAG TAT CTA CAG GTT TAT TCG TGT GGT GCG GGT CAG Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val> AAA TTA CTT AGA GGC CAT ACT CTT GTC CTC AAT TGT ACT GCT ACC ACT CCC TTG AAC ACG TTT AAT GAA TCT CCG GTA TGA GAA CAG GAG TTA ACA TGA CGA TGG TGA GGG AAC TTG TGC Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr> AGA GTT CAA ATG ACC TGG AGT TAC CCT GAT GAA AAA AAT AAG AGA GCT TCC GTA AGG CGA TCT CAA GTT TAC TGG ACC TCA ATG GGA CTA CTT TTT TTA TTC TCT CGA AGG CAT TCC GCT Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys Asn Lys Arg Ala Ser Val Arg Arg> CGA ATT GAC CAA AGC AAT TCC CAT GCC AAC ATA TTC TAC AGT GTT CTT ACT ATT GAC AAA GCT TAA CTG GTT TCG TTA AGG GTA CGG TTG TAT AAG ATG TCA CAA GAA TGA TAA CTG TTT Arg Ile Asp Gln Ser Asn Ser His Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys> ATG CAG AAC AAA GAC AAA GGA CTT TAT ACT TGT CGT GTA AGG AGT GGA CCA TCA TTC AAA TAC GTC TTG TTT CTG TTT CCT GAA ATA TGA ACA GCA CAT TCC TCA CCT GGT AGT AAG TTT Met Gln Asn Lys Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys> TCT GTT AAC ACC TCA GTG CAT ATA TAT GAT AAA GCA GGC CCG GGC GAG CCC AAA TCT TGT AGA CAA TTG TGG AGT CAC GTA TAT ATA CTA TTT CGT CCG GGC CCG CTC GGG TTT AGA ACA Ser Val Asn Thr Ser Val His Ile Tyr Asp Lys Ala Gly Pro Gly Glu Pro Lys Ser Cys> GAC AAA ACT CAC ACA TGC CCA CCG TGC CCA GCA CCT GAA CTC CTG GGG GGA CCG TCA GTC CTG TTT TGA GTG TGT ACG GGT GGC ACG GGT CGT GGA CTT GAG GAC CCC CCT GGC AGT CAG Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val> DRAFTSK:



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Fig.10C.

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						CCC													
						GGG													
Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	met	тте	ser	Arg	Thr	Pro	GIU	vaı	TILL>
		115	: n		1 1	160		-	170			118	30		11	.90		1	200
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TGC	GTG	GTG	GTG	GAC	GTG	AGC	CAC	GAA	GAC	CCT	GAG	GTC	AAG	TTC	AAC	TGG	TAC	GTG	GAC
						TCG													
																			Asp>
-				_															
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	*		*	*		*		*	. *		*		*	*		*		*	*
						GCC													
CCG	CAC	CTC	CAC	GTA	TTA	CGG	TTC	TGT	TTC	GGC	GCC	CTC	CTC	GTC	ATG	TTG	TCG	TGC	ATG
Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr>
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						TGG													
Ara	Val	Val	Ser	Val	Len	ጥክ ተ	Val	Leu	His	Gln	Asp	Tro	Leu	Asn	Glv	Lvs	Glu	Tyr	Lys>
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						GCC													
ACG	TTC	CAG	AGG	TTG	TTT	CGG	GAG	GGT	CGG	GGG	TAG	CTC	TTT	TGG	TAG	AGG	TTT	CGG	$T_{n}T_{n}T_{n}$
Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys>
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						GTC													
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						TGC													
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GAC	GGC	TCC	TTC	TIC	CTO	TAC	C AG	AA C	G ĆTY	CAC	CGTY	G GA	C AAC	G AG	C AGO	G TG(	G CAC	CAC	GGG
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Asp	Gly	Ser	Phe	e Phe	e Lev	ı Ty	r Se	r Ly	s Le	u Th	r Va	l As	p Ly:	s Se	r Ar	g Tr	o Gli	ı Gl	n Gly

ORAFTSHAME



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#### Fig. 10D.

1690 1700

CTC TCC CTG TCT CCG GGT AAA TGA GAG AGG GAC AGA GGC CCA TTT ACT Leu Ser Leu Ser Pro Gly Lys ***

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ORAFISIA

Fig. 11

Intracellular kinase 1151 domain 926 994 Transmembrane 812 687 750759 unique 31 a.a. eN  $\frac{1}{8}$ 9°7° 98 Extracellular ligand binding 550 NS. 5 s 5.5 5 457 4 N domains 4 4 4 345 38 က္ခ် က္ရွိ က္ရွိ 23 230 230 S. S. 7N SFIt-1 SP Human FLT-1 SP 6N sFlt-1 SP Amino acid No.1 13\28

c-terminus

5

4

က္ရွိ

N_s

5N sFIt-1 SP

က္ရွိ

4N sFIt-1 SP-

 $\mathfrak{C}$ N_s 3N SFIt-1 SP

2N sFIt-1 SP



DRAFTSE.



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#### Fig. 13A

				ıg.	73	SA	•												
		1	0	_		20			30			4	0			50			60
3 m/C	*	200	* m>~	*	CAC	*		*	*	CWC	алст. *	ccc	*	* Cmc	אככ	ux⊐ur *	Carc	<b>८७७</b> ★	<b>СПС</b>
				TGG ACC															
																	•		Leu>
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	*	•	*	*		*		*	*		*	10	*	*	-	*		*.	*
				TCA															
				AGT		•													GTC Gln>
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				GCA															
				CGT															rii.
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		19	90		2	200		-	210			22	20		:	230			240
<b>m</b> cc	<b>~</b>	mm>	*	* GAA	2000	*	N C III	* * * * * * * * * * * * * * * * * * * *	~ ×	NGC	CD D	NCC.	Cux:	אכר	מיזימ	אריטע ×	מממ	עלטער ×	GCC *
				CTT															
																			Ala>
_																			
	*			*		260 *		*					80 *			290 *		*	300 *
TGT				GGC															
				CCG															
Cys	Gly	Arg	Asn	Gly	Lys	Gln	Phe	Cys	Ser	Thr	Leu	Thr	Leu	Asn	Thr	Ala	Gln	Ala	Asn>
		31	10		:	320			330			3	40			350			360
	*		*	*		*		*	*		*		*	*	•	*		*	*
																			ACA
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GAA	ATC	CCC	GAA	ATT	ATA	CAC	ATG	ACT	GAA	GGA	AGG	GAG	CTC	GTC	TTA	, GCC	TGC	CGG	GTT
												•							CAA
Glu	Ile	Pro	Glu	Ile	Ile	His	Met	Thr	Glu	Gly	Arg	Glu	Leu	Val	Ile	Pro	Cys	Arg	Val>
		4	90			500			510			5	20			530			540
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71'h~	Ser	Pro	Asn	TTE	LUX	val	. Thr	ren	rhys	rys	⊾ ⊾ue	: Pro	ner	. AST	) INI	. net	1 TTE	: PIC	Asp>



## Fig.13B.

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G.	ly :	Lys	Arg	Ile	Ile	Trp	Asp	Ser	Arg	Lys	Gly	Phe	Ile	Ile	Ser	Asn	Ala	Thr	Tyr	Lys>
						_				<b>620</b>						_				660
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		-	7	30		,	740			750	•		76	60			770			780
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A	AA	TTA	CTT	AGA	GGC	CAT	ACT	CTT	GTC	CTC	AAT	TGT	ACT	GCT	ACC	ACT	CCC	TTG	AAC	ACG
														CGA						
L	ys	Leu	Leu	Arg	Gly	His	Thr	Leu	Val	Leu	Asn	Cys	Thr	Ala	Thr	Thr	Pro	Leu	Asn	Thr>
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			c	10			920			930	<b>)</b>		9	40			950			960
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C	Суs	Arg	Val	Arg	s Ser	Gly	Pro	Ser	Phe	Lys	Ser	Val	l Asn	Thr	Ser	· Val	His	; Ile	ne Ty:	r Asp>
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Fig. 13C.

CTC ATG ATC TCC CGG ACC CCT GAG GTC ACA TGC GTG GTG GTG GAC GTG AGC CAC GAA GAC GAG TAC TAG AGG GCC TGG GGA CTC CAG TGT ACG CAC CAC CAC CTG CAC TCG GTG CTT CTG Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp> CCT GAG GTC AAG TTC AAC TGG TAC GTG GAC GGC GTG GAG GTG CAT AAT GCC AAG ACA AAG GGA CTC CAG TTC AAG TTG ACC ATG CAC CTG CCG CAC CTC CAC GTA TTA CGG TTC TGT TTC Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys> CCG CGG GAG GAG CAG TAC AAC AGC ACG TAC CGT GTG GTC AGC GTC CTC ACC GTC CTG CAC GGC GCC CTC CTC GTC ATG TTG TCG TGC ATG GCA CAC CAG TCG CAG GAG TGG CAG GAC GTG Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His> CAG GAC TGG CTG AAT GGC AAG GAG TAC AAG TGC AAG GTC TCC AAC AAA GCC CTC CCA GCC GTC CTG ACC GAC TTA CCG TTC CTC ATG TTC ACG TTC CAG AGG TTG TTT CGG GAG GGT CGG Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala> CCC ATC GAG AAA ACC ATC TCC AAA GCC AAA GGG CAG CCC CGA GAA CCA CAG GTG TAC ACC GGG TAG CTC TTT TGG TAG AGG TTT CGG TTT CCC GTC GGG GCT CTT GGT GTC CAC ATG TGG Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr> CTG CCC CCA TCC CGG GAT GAG CTG ACC AAG AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GAC GGG GGT AGG GCC CTA CTC GAC TGG TTC TTG GTC CAG TCG GAC TGG ACG GAC CAG TTT Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys> GGC TTC TAT CCC AGC GAC ATC GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC CCG AAG ATA GGG TCG CTG TAG CGG CAC CTC ACC CTC TCG TTA CCC GTC GGC CTC TTG TTG Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn> TAC AAG ACC ACG CCT CCC GTG CTG GAC TCC GAC GGC TCC TTC TTC CTC TAC AGC AAG CTC ATG TTC TGG TGC GGA GGG CAC GAC CTG AGG CTG CCG AGG AAG AAG GAG ATG TCG TTC GAG Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu> ACC GTG GAC AAG AGC AGG TGG CAG CAG GGG AAC GTC TTC TCA TGC TCC GTG ATG CAT GAG TGG CAC CTG TTC TCG TCC ACC GTC GTC CCC TTG CAG AAG AGT ACG AGG CAC TAC GTA CTC Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu>

#### Fig. 13D.

GCT CTG CAC AAC CAC TAC ACG CAG AAG AGC CTC TCC CTG TCT CCG GGT AAA TGA CGA GAC GTG TTG GTG ATG TGC GTC TTC TCG GAG AGG GAC AGA GGC CCA TTT ACT Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys ***>

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#### Fig.14A.

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Thr	Cys	Glu	Ala	Thr	Val	Asn	Gly	His	Leu	Tyr	Lys	Thr	Asn	Tyr	Leu	Thr	His	Arg	Gln>
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Fig.14B.

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						CAA														
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Glu	Pro	Lys	Ser	Cys	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Суѕ	Pro	Ala	Pro	Glu	Leu	Leu>	
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Ile	Ser	Lys	Ala	Lys	Gl)	/ Glr	Pro	Arg	g Glu	ı Pro	o Glr	ı Val	ι Туз	Th	r Le	u Pr	o Pr	o Se	r Arg;	>
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#### Fig. 14C.

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

	SAT GAG CTG ACC CTA CTC GAC TGG Asp Glu Leu Thr  1150  * SAC ATC GCC GTG CTG TAG CGG CAC			11	.00		1	110			112	0.0		11	30		1	140	
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GAT	GAG	CTG	ACC	AAG	AAC	CAG	GTC	AGC	CTG	ACC	TGC	CTG	GTC	AAA	GGC	TTC	TAT	CCC	AGC
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CTG	TAG	CGG	CAC	CTC	ACC	CTC	TCG	TTA	CCC	GTC	GGC	CTC	TTG	TTG	ATG	TTC	TGG	TGC	GGA
Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro>
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GGG	CAC	GAC	CTG	AGG	CTG	CCG	AGG	AAG	AAG	GAG	ATG	TCG	TTC	GAG	TGG	CAC	CTG	TTC	TCG
Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser>
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TCC	ACC	GTC	GTC	CCC	TTG	CAG	AAG	AGT	ACG	AGG	CAC	TAC	GTA	CIC	CGA N3-	GAC	GIG	7.1.0	GTG
Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	ser	vaı	met	HIS	GIU	Ala	Leu	nis	ASII	His>
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### Fig.15A.

ATG GTC AGC TAC TGG GAC ACC GGG GTC CTG CTG TGC GCG CTG CTC AGC TGT CTG CTT TAC CAG TGG ATG ACC CTG TGG CCC CAG GAC GAC GAC GAC GAC GAC GAC G						9.	10	<i>,</i>									·			
ATG GTC AGC TAG TAG GAC ACC GGG GTC CTG CTG TGC GGG CTG CTC AGC TGT CTG CTT TAC CAG TCG ATG ACC CTG TGG CCC CAG GAC GAC GAC GAC GAC GAC GAC G			1	.0			20			30			4		•		50			60
THE CAG TROS ATT ACC CITE TOS CCC CAG GAC ACA CAG CGC GAC GAG ATT GACA GAC GAC MET VAI SET TYY TYP ASP THY Gly Val Leu Leu Cys Ala Leu Leu Ser Cys Leu Leu 70 80 90 100 110 110 10 100 110 100 100 110 100 100 110 100 100 110 100 100 100 110 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100 100	».m∕~	*	<b>&gt;</b>			C2 C					Carc		CCC			אככ		CITC		· *
Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser Cys Leu Leu  70 80 90 100 110  ACA GGA TCT AGT TCC GGA GGT AGA CCT TTC GTA GAG ATG TAC AGT GAA ATC CCC GAA TGT CCT AGA TCA AGG CCT CCA TCT GGA AAG CAT CTC TAC ATG TCA CTT TAG GGG CTT Thr Gly Ser Ser Ser Gly Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu  130 140 150 160 170  ATA CAC ATG ACT GAA GGA AGG GAG CTC GTC ATT CCC TGC CGG GTT ACG TCA CAT GAA TTC TAT GTC TAC TGA CTT CCT TCC CTC GAG CAG TAA GGG ACG CCC CAA TGC AGT GGA ATG TAT GTC TAC TGA CTT CCT TCC CTC GAG CAG TAA GGG ACG CCC AAA TGC AGT GGA TTC Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asr  190 200 210 220 230  ACT GTT ACT TTA AAA AAG TTT CCA CTT GAC ACT TTG ATC CCT GAT GGA AAA CCA ATT TGA CAA TGA AATT TTT TTC AAA GGT GAA CTT GAC ACT TTG ATC CCT GAT GGA AAA CCA ATT TGA CAA TGA AATT TTT CAAA GGT GAA CTT GAC ACT TGA ACC TAG GGA CAT ACCT TTG CAG TAT TGA CAA TGA AATT TTT CAAA GGT GAA CTT GAC ACT TGG ACC ACT ACC CTT TTA CAG TAT TCA CAA TGA AAG GGC TTC ATC ATC ATA TCA AAT GCA ACG TAC AAA GAA ATA CCC TTT TAC CCC AAG TTCA CCT TCC TCC CCG AAG TAG TAT AGT TTA CGT TGC ATG TTT CTT TAT CCC GAA TCC CTG TCA TCT TTC CCG AAG TAG TAT AGT TTA CGT TGC ATG TTT TTT TAT CCC GAA TTP ASP Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Lee  310 320 330 340 350  ACC TGT GAA GCA ACA GTC AAT GGG CAT TTG TAT AAT TCT TAT TAT CCC GAA TGG ACA CTT CGT TGT CAG TTA CCC GTA AAC ATA TTC TGT TTG ATA GAG TGT GTA TGG TAT TGT TAG CAG TTA CCC GTA AAC ATA TTC TGT TTG ATA GAG TGT GTA TGG TAT TGT TAG TAT CAG GTT ACC GTA AAC ATA TTC TGT TTG ATA GAG TGT GTA TGT TAG TAT TGT TAG TAT CCC GTA AAC ATA TTC TGT TGT AAC ACT CTC TTG AAC ACT TGT TGT CAG TTT TAT TCC GTA GAG ACC CCC CGC CAG GTC AAA TTA CTT ACC GTA TTT ACT TTT TTT TAT CTT TTT TAT CTT TAT TCT TGT TTG TTG TAG TAT TGT TAG TAT CTC AAA TTA CTT ACC GTT TAT TCT GTT TGT TGT TAG TAT TGT TAG TAT TGT TAG TAT TGT TAG TTG TAT TCT TGT TGT CAG TTT TAT TCT TGT TGT TGT TAG TAT TGT TAG TTT TTT TAT CCT GAT TTT TTT TTT TTT TTT TTT TTT TTT TT																				
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* * * * * * * * * * * * * * * * * * *	.r.tb	Asp	Ser	Arg	Lys	GIĀ	Pne	iie	тте	Ser	Asn	Ala	THE	TYT	гÀг	GIU	ııe	GIĀ	ren	ren>
ACC TGT GAA GCA ACA GTC AAT GGG CAT TTG TAT AAG ACA AAC TAT CTC ACA CAT CG TGG ACA CTT CGT TGT CAG TTA CCC GTA AAC ATA TTC TGT TTG ATA GAG TGT GTA GC Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Ar  370 380 390 400 410  * * * * * * * * * * * * * * * * * * *			3	10			320			330			3	40			350			360
TGG ACA CTT CGT TGT CAG TTA CCC GTA AAC ATA TTC TGT TTG ATA GAG TGT GTA GCC Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Ar  370 380 390 400 410  * * * * * * * * * * * * * * * * * * *																				
Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arman Tyr Tyr Leu Thr His Arman Tyr Tyr Leu Thr His Arman Tyr Tyr Leu Tyr Lys Thr Asn Tyr Leu Tyr Lys Tyr Lys Tyr Lys Thr Asn Tyr Leu Tyr Lys																				
370 380 390 400 410  * * * * * * * * * * * * * * * * * * *										-										
* * * * * * * * * * * * * * * * * * *		_																		
ACC AAT ACA ATC ATA GAT GTC CAA ATA AGC ACA CCA CGC CCA GTC AAA TTA CTT AGT TGG TTA TGT TAG TAT CTA CAG GTT TAT TCG TGT GGT GCG GGT CAG TTT AAT GAA TCA TAR ASN Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val Lys Leu Leu Argan Acc Acc Cat Cct Gat Gat Gat Gat Gat Gat Gat Gat Gat Ga		*																		420 *
TGG TTA TGT TAG TAT CTA CAG GTT TAT TCG TGT GGT GCG GGT CAG TTT AAT GAA TCT Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val Lys Leu Leu Argental Ash	ACC																			
430 440 450 460 470  * * * * * * * * * * * * * * * * * * *	TGG	TTA	TGT	TAG	TAT	CTA	CAG	GTT	TAT	TCC	TGT	GGI	GCG	GGI	' CAG	TTI	מא י	GAA	TCI	, CCG
CAT ACT CTT GTC CTC AAT TGT ACT GCT ACC ACT CCC TTG AAC ACG AGA GTT CAA AT GTA TGA GAA CAG GAG GTT AACA TGA CGA TGG TGA GGG AAC TTG TGC TCT CAA GTT TA His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr Arg Val Gln Me 490 500 510 520 530 530 530 530 530 530 530 530 530 53	Thr	Asn	Thr	Ile	Ile	asp	Val	Gln	Ile	e Ser	Thr	Pro	Arg	Pro	Val	Lys	s Leu	ı Lev	Arg	Gly>
CAT ACT CTT GTC CTC AAT TGT ACT GCT ACC ACT CCC TTG AAC ACG AGA GTT CAA AT GTA TGA GAA CAG GAG TTA ACA TGA CGA TGG TGA GGG AAC TTG TGC TCT CAA GTT TA His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr Arg Val Gln Met 490 500 510 520 530 530 76G AGT TAC CCT GAT GAA AAA AAT AAG AGA GCT TCC GTA AGG CGA CGA ATT GAC CAA ATT GAC ATT			4	30			440	•		450	)		4	160			470			480
GTA TGA GAA CAG GAG TTA ACA TGA CGA TGG TGA GGG AAC TTG TGC TCT CAA GTT TA His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr Arg Val Gln Me 490 500 510 520 530				*			*												*	*
His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr Arg Val Gln Me  490 500 510 520 530  * * * * * * * * * * * * *  TGG AGT TAC CCT GAT GAA AAA AAT AAG AGA GCT TCC GTA AGG CGA CGA ATT GAC CX																				
490 500 510 520 530 * * * * * * * * * * * * *  TGG AGT TAC CCT GAT GAA AAA AAT AAG AGA GCT TCC GTA AGG CGA CGA ATT GAC CA																				
* * * * * * * * * * * * * * * * * * *							- <b>,</b>												_	
TGG AGT TAC CCT GAT GAA AAA AAT AAG AGA GCT TCC GTA AGG CGA CGA ATT GAC C			. 4	90		<b>.</b>			•			ąż.	ţ	520		•	530		•	540 *
	TGG	AGT	י ייאַר	י כיריו ג				<u>ነ</u> ይልባ	- ' <u>A</u> A				GT	A AG	G CGA	A CG	^ А АТ	T GA	C CA	A AGC

Trp Ser Tyr Pro Asp Glu Lys Asn Lys Arg Ala Ser Val Arg Arg Arg Ile Asp Gln Ser>

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## Fig.15B.

																			-	
1			55	50		5	60			570			58	30		5	90			600
		*		*	*		*		*	*		*		*	*	Ī	*		*	*
	TAA	TCC	CAT	GCC	AAC	ATA	TTC	TAC	AGT	GTT	CTT	ACT	TTA	GAC	AAA	ATG	CAG	AAC	AAA	GAC
	TTA	AGG	GTA	CGG	TTG	TAT	AAG	ATG	TCA	CAA	GAA	TGA	TAA	CTG	TTT	TAC	GTC	TTG	$\mathbf{T}\mathbf{T}\mathbf{T}$	CTG
	ASI	Ser	HIS	Ala	Asn	Ile	Phe	TYY	Ser	Val	Leu	Thr	Ile	Asp	Lys	Met	Gln	Asn	Lys	Asp>
		*	63	10		6	520		*	630		*	64			6	550			660
	AAA	GGA	للملت		תים ב	መረታጥ	CGT	CTA		 	CCA		πς λ	* mm>	*	<b>~~</b>	*		*	*
	TrTrT	CCT	GAA	ATA	TGA	ACA	GCA	CAT	400	TOA	CCT.	CCA	DCT.	TIC	WAY.	TCT	GTT.	AAC	ACC	TCA
	Lys	Gly	Leu	Tyr	Thr	Cys	Arg	Val	Arg	Ser	Gly	Pro	Ser	Phe	Lys	Ser	Val	Asn	Thr	Ser>
				70			580			690							•			
		*	•	*	*	,	*		*	09U *		*	/ (	, ,	*	1	710		<b>-</b>	720
	GTG	CAT	ATA	TAT	GAT	AAA	GCA	GGC	CCG	GGC	GAG	CCC	AAA	th.	ىلىڭىلى	GAC	ה מממ	ъ <del>Ст</del> п	CNC	ה ארש
							CGT													
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		*	′ -	*	*		*		*	, 5U *		*	. / (	50 ★	*		770 *			780
	TGC	CCA	CCG	TGC	CCA	GCA	CCT	GAA	CTC	CTG	GGG	GGA	CCG	TCA	האגה "	مكلعل	Cıi∧. 	ייעועין	CCC	CCD
	ACG	GGT	GGC	ACG	GGT	CGT	GGA	CTT	GAG	GAC	CCC	CCT	GGC	AGT	CAG	AAG	GAG	DAG	CCC	CCA
	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro>
			7	90		5	800			810			0	20		,	220			242
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							ATG													
	TTT	GGG	TTC	CTG	TGG	GAG	TAC	TAG	AGG	GCC	TGG	GGA	CTC	CAG	TGT	ACG	CAC	CAC	CAC	CTG
	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp>
			8	50		1	860			870			88	80		;	890			900
	بيسي	*	C2 C	*	*		*		*	*		*		*	*		*		*	*
							GAG													
	Val	Ser	His	Glu	Yen	Pro	CTC	17=1	TAC	AAG Dho	116	ACC m~~	AIG	CAC	CTG	CCG	CAC	CIC	CAC	GTA His>
					ليونده		GTU	AGT	אַעניי	FIIE	nsii	ıτħ	TÄE	val	ASP	стλ	va1	GIU	val	H1\$>
		*	9:	10 *	*		920 *		*	930 *		*	9	40 *	*	!	950 *		*	960 *
	AAT	GCC	AAG	ACA	AAG	CCG	CGG	GAG	GAG	CAG	TAC	AAC	AGC	ACG	TAC	CGT	GTG	GTC	AGC	GTC
	TTA	CGG	TTC	TGT	TTC	GGC	GCC	CTC	CTC	GTC	ATG	TTG	TCG	TGC	ATG	GCA	CAC	CAG	TCG	CAG
	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val>
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		*		*	*		*		*			*		*	*		*			. *
	CTC	ACC	GTC	CTG	CAC	CAG	GAC	TGG	CTG	AAT	GGC	AAG	GAG	TAC	AAG	TGC	AAG	GTC	TCC	AAC
	GAG	TGG	CAG	GAC	GTG	GTC	CTG	ACC	GAC	TTA	CCG	TTC	CTC	ATG	TTC	ACG	TTC	CAG	AGG	TTG
	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn>
			10	30	•	1	040			1050			10	60		1	070			1080
		* .		*	*		*		*	*		*		*	*		*		*	*
	AAA	GCC	CTC	CCA	GCC	CCC	ATC	GAG	AAA	ACC	ATC	TCC	AAA	GCC	AAA	GGG	CAG	CCC	CGA	GAA
	TTT	CGG	GAG	GGT	CGG	GGG	TAG	CTC	TTT	TGG	TÁG	AGG	TTT	CGG	TTT	CCC	GTC	GGG	GCT	CTT
	₽∧2	wra	rėn	Pro	Ala	Pro	Ile	·Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu>



#### Fig.15C.

1140 1130 1120 1110 1100 1090 CCA CAG GTG TAC ACC CTG CCC CCA TCC CGG GAT GAG CTG ACC AAG AAC CAG GTC AGC CTG GGT GTC CAC ATG TGG GAC GGG GGT AGG GCC CTA CTC GAC TGG TTC TTG GTC CAG TCG GAC Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu> 1200 1190 1180 1170 1160 1150 ACC TGC CTG GTC AAA GGC TTC TAT CCC AGC GAC ATC GCC GTG GAG TGG GAG AGC AAT GGG TGG ACG GAC CAG TTT CCG AAG ATA GGG TCG CTG TAG CGG CAC CTC ACC CTC TCG TTA CCC Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly> 1260 1250 1230 1240 1210 1220 CAG CCG GAG AAC AAC TAC AAG ACC ACG CCT CCC GTG CTG GAC TCC GAC GGC TCC TTC TTC GTC GGC CTC TTG TTG ATG TTC TGG TGC GGA GGG CAC GAC CTG AGG CTG CCG AGG AAG AAG Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe> 1320 1310 1300 1270 1280 CTC TAC AGC AAG CTC ACC GTG GAC AAG AGC AGG TGG CAG CAG GGG AAC GTC TTC TCA TGC GAG ATG TCG TTC GAG TGG CAC CTG TTC TCG TCC ACC GTC GTC CCC TTG CAG AAG AGT ACG Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys> 1380 1370 1360 1350 1340 1330 TCC GTG ATG CAT GAG GCT CTG CAC AAC CAC TAC ACG CAG AAG AGC CTC TCC CTG TCT CCG AGG CAC TAC GTA CTC CGA GAC GTG TTG GTG ATG TGC GTC TTC TCG GAG AGG GAC AGA GGC Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro> GGT AAA TGA CCA TTT ACT Gly Lys ***>

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# Fig. 16A.

		1	.0			20			30			4	0			50			60
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ATG																			
TAC	CAG	TCG	ATG	ACC	CTG	TGG	CCC	CAG	GAC	GAC	ACG	CGC	GAC	GAG	TCG	ACA	GAC	GAA	GAG
Met	Val	Ser	Tyr	Trp	Asp	Thr	Gly	Val	Leu	Leu	Cys	Ala	Leu	Leu	ser	Cys	Leu	Leu	Leu>
		•	70			80			90			10	00		1	.10			120
	*	,	*	*		* .		*	*		*	-	*	*	_	*		*	*
ACA	GGA	TCT	AGT	TCA	GGT	TCA	AAA	ATT	AAA	GAT	CCT	GAA	CTG	AGT	ATT	AAA	GGC	ACC	CAG
TGT	CCT	AGA	TCA	AGT	CCA	AGT	TTT	TAA	$\mathbf{T}\mathbf{T}\mathbf{T}$	CTA	GGA	CTT	GAC	TCA	TAA	TTT	CCG	TGG	GTC
Thr	Gly	Ser	Ser	Ser	Gly	Ser	Lys	Leu	Lys	Asp	Pro	Glu	Leu	Ser	Leu	Lys	Gly	Thr	Gln>
												-	<b>.</b> .		4	. 7 ^			100
		13	30:		1	.40		*	.150		*	10	60 *	*	1	L70 ★		*	180
CNC	» ж	א מער	* ~~~	* CC3	GGC	<b>*</b>	מסמ			ריזער		TGC	AGG		GAA	GCA	GCC	САТ	AAA
CAC	MAG	TAC	CAA	CCT	CCG	GTC	TGT	GAC	GTA	GAG	GTT	ACG	TCC	CCC	CTT	CGT	CGG	GTA	TTT
His	Ile	Met	Gln	Ala	Gly	Gln	Thr	Leu	His	Leu	Gln	Cys	Arg	Gly	Glu	Ala	Ala	His	Lys>
					-														
		1	90		2	200			210			. 2	20		:	230			240
	*		*	*		*		*	*		*		· *	*		*		*	*
TGG	TCT	TIG	CCT	GAA	ATG	GTG	AGT	AAG	GAA	AGC	GAA	AGG	CIG	AGC	ATA	ACT	AAA	TCT	CGG
ACC	AGA	AAC	GGA	CTT	TAC	CAC	TCA	TIC	CIT	TCG	Glu	Ara	TAU	Ser	TAL	TGA	INS	Ser	Ala>
Trp	ser	.Leu	PIO	GIU	met	vai	Ser	гу	GIU	261	GIU	ALG	عات ا	502	110	++11	ت رح	502	
		2	50		;	260			270			2	80			290			300
	*	_	* .	*		*		*	*		*		*	*		*		*	*
					AAA														
ACA	CCT	TCT	TTA	CCG	TTT	GTT	AAG	ACG	TCA	TGA	TAA	TGG	AAC	TTG	TGT	CGA	GTT	CGT	TTG
Cys	Gly	Arg	Asn	Gly	Lys	Gln	Phe	Cys	Ser	Thr	Leu	Thr	Leu	Asn	Thr	Ala	Gin	Ala	Asn>
		3	10			220			330	)			40			350			360
	. *	3	10	*		320		*	*		*		*	*		*		*	*
CAC		GGC				TGC	AAA	TAT	CTA	GCI	GTA	CCI	ACI	TCA	AAG	AAG	AAG	GAA	ACA
GTG	TGA	CCG	AAG	ATC	TCG	ACG	TTT	ATA	GAT	CGA	CAT	GGA	I TGA	AGT	TIC	TTC	TTC	CTI	TGT
His	Thr	Gly	Phe	Тут	Ser	Cys	Lys	Tyr	Leu	Ala	val	Pro	Thr	Ser	. Lys	Lys	Lys	Glu	Thr>
																44.0		•	400
		3	70			380		*	390	) ∗	*		100 *	*		410 *		*	420 *
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Glu	Sex	Ala	Ile	· Tvi	Ile	Phe	Ile	Se	c Ası	o Thi	r Gly	Arg	g Pro	Phe	e Val	l Gl	ı Met	туз	r Ser>
				- 4															
		4	130			440			45				460	•	<u>.</u>	470			480
	*		*		k	*					*		*		k Danot	. * D 00	~ m~	.* ~ ~~/	*
GAA	YTA	CCC	GAA	ATT	T ATA	CAC	OTA :	AC'	r GA	A GG	A AG(	GA(	G CM	י האר ב ריאר	י איזיי גאיזי ב	7. CC	2 2C	2 GC	G GTT
CTT	TAC	GG(	s CT	r TAZ	A TAT	7 52.1.C	TA(	- 440-	r Cl	י בטי	r ICC	a Gi	u I.e.	ı Va	l Ile	e Pr	o Cv	s Ar	C CAA g Val>
GIU	· IIE	=. <b>P</b> 1(	ובט כ	v TT6	= TT6	- mis	, ME	- 444			,;	. <b></b>			. <b></b>	<b>-</b>			_
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	*		*		*	*		*		*	*		*		*	*		*	*
ACG	TC	A CC	AA T	YEA C	CAC	r GT	r AC	r <b>T</b> T	A AA	A AA	G TT	T CC	A CT	T GA	C AC	T.TT	G AT	c cc	T GAT
TGC	AG	r GGZ	YPT A	G TA	G TG	A CA	A TG	A AA	T TT	T TT	C AA	A GG	'I' GA	A CTV	G TG ∽ m⊾	A AA	C TA	G GG - D~	A CTA
Thr	Se	r Pro	o Ası	n Il	e Th	r Va	ı Th	r re	u Lý	s ry	s PN	e PI	O DE	u AS	נוג יו	בינו זי	لل يس:	u PI	o Asp>



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## Fig.16B.

					<b>J</b>	<del></del>													
		55	. ^		5	60	,		570			58	30		5	90			600
•	*	55	*	*	ر	*		*	*		*	5.	*	*	_	*		*	*
GGA Z	AAA	CGC	ATA	ATC	TGG	GAC	AGT	AGA	ÄAG	GGC	TTC	ATC	ATA	TCA	TAA	GCA	ACG	TAC	AAA
CCT '	$\mathbf{LLL}$	GCG	TAT	TAG	ACC	CTG	TCA	TCT	TTC	CCG	AAG.	TAG	TAT	AGT	TTA	CGT	TGC	ATG	TTT
Gly 1	Lys	Arg	Ile	Ile	Trp	Asp	Ser	Arg	Lys	Gly	Phe	Ile	Ile	Ser	Asn	Ala	Thr	Tyr	Lys>
•		61	LO		6	20			630			6	40		6	550		<b>.</b>	660
	*		*	*		*		*	*	~~~	*	000	*	*	m s m	*	202	770	* m>m
GAA .																			
CTT																			Tyr>
, Gau	TTG	GTA	reu	reu	THE	Cys	GIU	AIG	7111	var	ASII	G _x y	1110		-1.	<i></i> .			- <u></u>
		6	70		. 6	580			690			7	00			710			720
	*		*	*	Ì	*		*	*		*		*	*		, <b>*</b>		*	*
													ATA						
GAG	TGT	GTA	GCT	GTT	TGG	TTA	TGT	TAG	TAT	CTA	CAG	GTT	TAT	TCG	TGT	GGT	GCG	GGT	CAG
Leu	Thr	His	Arg	Gln	Thr	Asņ	Thr	Ile	Ile	Asp	Val	Gln	Ile	Ser	Thr	Pro	Arg	Pro	Val>
												-	<b>50</b>			770			700
	.4.	7	30	_		740			750		*	,	60 *			770 *		*	780 *
***	mm y	CMM	* >~	~	Cam	× ×∽m	Cum	Cux-	CUC.	יחממ	44.54b	א Cית	GCT	ACC	ACΨ	CCC	באנית	AAC	ACG
													CGA						
																			Thr>
2,2	200	204	9	Q L J	1120	••••	200												
•		7	90			800			810	)		8	320			830			840
	* .		*	*		*		*					*			*		*	*
AGA	GTT	CAA	ATG	ACC	TGG	AGT	TAC	CCI	' GAI	GAA	AAA .	AA	DAA 7	AAC	GCI	TCC	GTA	AGC	CGA
TCT	CAA	GTT	TAC	TGG	ACC	TCA	ATG	GGA	CTA	CTI	r TTI	TT	\ TTC	TTG	CGA	AGG	CAT	TCC	GCT
Arg	Val	Gln	Met	Thr	Trp	Ser	Tyr	Pro	) Asr	Glu	ı Lys	s Asi	ı PAs	ASD	ALE	. Ser	val	. Arg	Arg>
-		0				860			870	1		5	380			890			900
	*	0	50 *	*				*			. *		*	*		*		*	*
CGA	ATT	GAC	CAA	AGC	raa :						TT	TA	C AG	GTI	CT	r aci	TA	GAO	AAA C
																			G TTT
Arg	Ile	Asp	Glr	Ser	Asr	Ser	His	: Ala	a Ası	n Ile	e Phe	e Ty	r Sei	. Val	. Le	ı Thi	: Ile	a Asy	p Lys>
		9	10			920			93		_		940		<b>r</b>	950		*	960 *
	*		*			*					*		* *						
																			C AAA G TTT
Met	GIV	. TIC	3 TAZ	r Cit	5 1-1". 5 TAK	$\mathbf{r} \in \mathbb{C}^n$	r GAZ	1 TV	ተ ጥክ	r Cv	s Ar	r Va	1 Arc	r Se	c Gl	v Pr	o Se	r Ph	e Lys>
riec	GII	i ASI	ı Ly.	. കാ	י אַנו י	s GI,	y De	~ <b>~</b> ~ ~ .		_ 0,		5		5					•
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Ser	Va.	l As	n Th	r Se	r Va	l Hi	s Il	е Ту	r As	b ry	s Al	a Gl	y Pr	o Gl	y Gl	u Pr	o Ly	s Se	er Cys>
		_	000			1010			105	: 0		4	060			1070		•	1080
	*	1	030		*	1040		*	105	*	*		±		*	±0/0	,	*	*
GAC		מ ב	ጥ ቦል.	ር አር	″ Δ ΨΥ⊇	ک . <i>د</i> ر پ	א רר	 	:C C	LA GC	A CC	T G	AA CT	יכ כיז	G GC	G GC	A CC	G TY	CA GTC
																			GT CAG
Asp	Ly	s Th	r Hi	s Th	r Cv	's Pr	o Pr	.o C	s Pi	co Al	a Pr	co G	lu Le	eu Le	u G	ly G	y Pi	co S	er Val>
-	-				-			_											



# Fig.16C.

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													TCC (						
													Ser						
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													AAG						
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	VAI	var	VAL	rop	V CL _	<b>5</b> 61.	1172	Gr.a	حوصد				27.0						E
		12:	10		12	20			L230			124	0		12	50		:	1260
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													GAG						
													CTC						
GiA	Val	GIU	Val	His	Asn	Ala	ГЛS	Thr	гĀг	Pro	Arg	GIU	GIU	GIN	TYL	ASII	ser	THE	TYY>
		12	70		12	280		;	1290			130	00		13	310			1320
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													CTG						
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Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	GIĀ	Lys	GIU	Tyr	Lys>
		13	30		1:	340			1350			13	60	,	13	370			1380
	*												*						
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Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys>
		12	90		٦.	400			1410			74	20		1.	430			1440
	*				Τ.								*						*
GGG	CAG	ccc	CGA	GAA	CCA	CAG	GTG	TAC	ACC	CTG	CCC	CCA	TCC	CGG	GAT	GAG	CTG	ACC	AAG
																			TTC
Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Тух	Thr	Leu	Pro	Pro	Ser	Arg	qzA	Glu	Leu	Thr	Lys>
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AAC	CAG															ATC	GCC	GTY	G GAG
TTG	GTC	CAG	TCG	GAC	TĢG	ACG	GAC	CAC	TI	, ccc	AAG	ATA	GGG	TCG	CTG	TAG	CGG	CA	CTC
Asn	Glr	val	Ser	Leu	Thr	Cys	Lev	val	Lys	Gly	Phe	тут	Pro	Ser	Asp	Ile	Ala	. Va	l Glu>
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TGO			*	*			GAC					ACC	ACG				CTG		C TCC
ACC	GAC	AGC	* C AAT	* GGG A CCC	CAG	: GG0	CTC	AA E	OAA C	CTAC	AAC	TĢC	TGC	CCI GGA	. GGC	GTG CAC	GAC	GA	C TCC G AGG
ACC	GAC	AGC	* C AAT	* GGG A CCC	CAG	: GG0	CTC	AA E	OAA C	CTAC	AAC	TĢC	TGC	CCI GGA	. GGC	GTG CAC	GAC	GA	
ACC	GAC	AGC TCC 1 Sei	* C AAT G TTA C Asr	* GGG A CCC	CAG GTC Gln	GGC GGC	CTO Glu	AA( TT( Asi	C AAC G TTC n Asr	TAC ATC	AAC	TGC Thi	TGC Thr	CCI GGA	GGC GGC Pro	GTG GAC Val	GAC	GA	G AGG p Ser>
ACC	GAC	AGC TCC 1 Sei	* C AAT	* GGG A CCC	CAG GTC Gln	: GG0	CTC Glu	AA( TT( Asi	C AAC G TTC n Asr 1590	TAC ATC TYI	AAC TTC	TGC Thi	TGC Thr	GGA Pro	GGC GGC Pro	GTG CAC	GAC	GA CT As	g agg
ACC	GAC CTC Glu	AGC TCC Ser	* C AAT C TTA C AST  570 *	* GGG	CAG GTC Gln	GCG GGG Pro	CTY Glu	AAC TTC 1 Asi	C AAC G TTC n Asr 1590	TAC ATC Tyi	AAC TTC Lys	TGC Thi	TGC Thr	CCI GGA Pro	GGC GGC Pro	GTO CAC Val	GAC	GAACT AS	G AGG p Ser> 1620
ACC Trr GAC CTC	GAC CTC Glv *	AGO TCC Ser 15 TCC AGO	* C AAT C AST  570 * C TTC G AAC	C TTC	GAG GTC Gln	GCG GGG Pro .580 *	C AGG	AAC AAC TTY AAC TTY	C AAC TTC A Asr 1590	TAC ATC Ty:	AAC TTC Lys *	TGC Thi 16 G GAC	Thr 500 * C AAC G TTC	GGA Pro	GGC GGC Pro	GTG CAC Val	GAC Lev GCAC	G GAG CTN AS CA CGT	G AGG p Ser> 1620



## Fig. 16D.

1630 1640 1650 1660 1670 1680

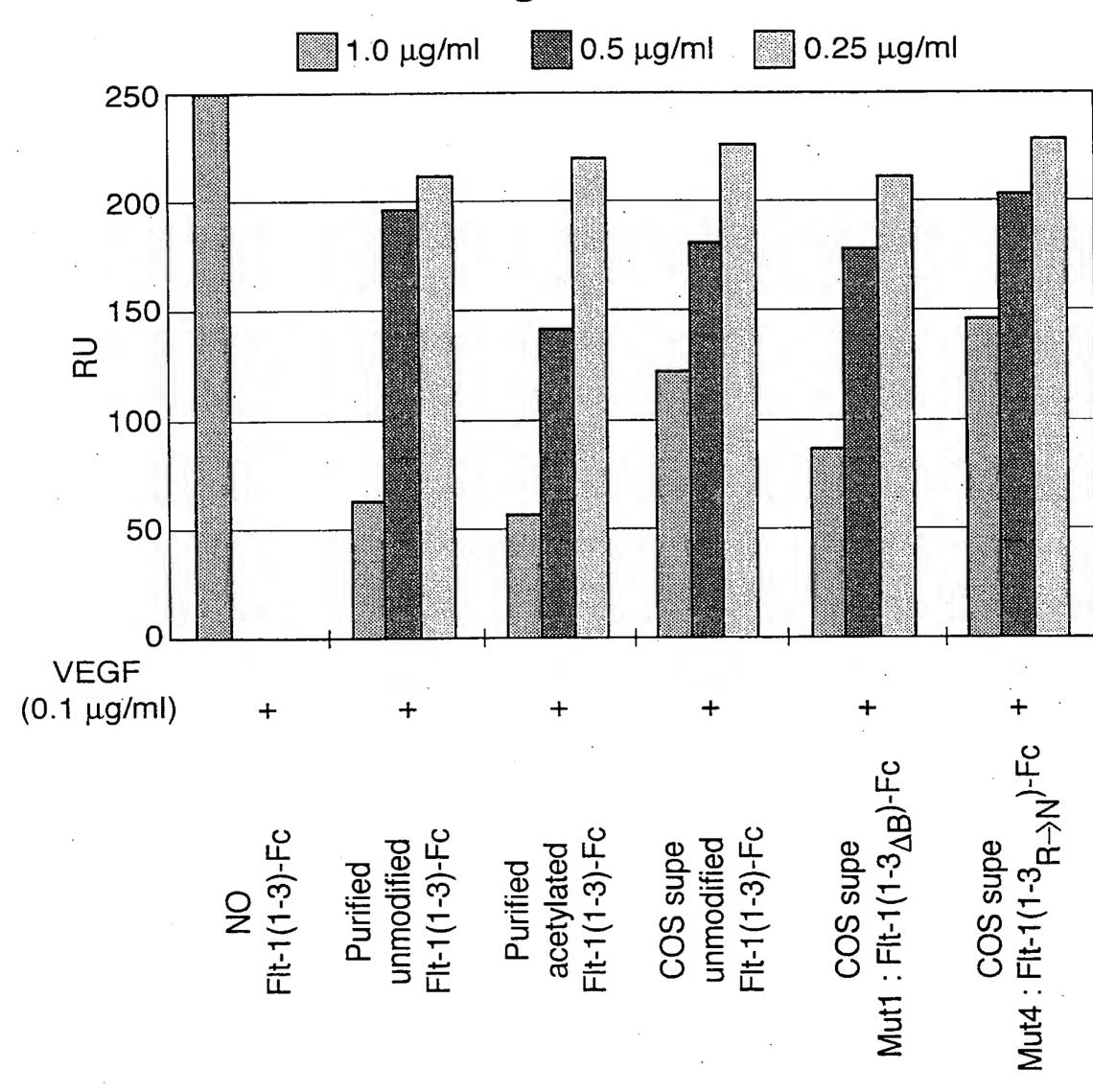
AAC GTC TTC TCA TGC TCC GTG ATG CAT GAG GCT CTG CAC AAC CAC TAC ACG CAG AAG AGC TTG CAG AAG AGT ACG AGG CAC TAC GTA CTC CGA GAC GTG TTG GTG ATG TGC GTC TTC TCG Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser>

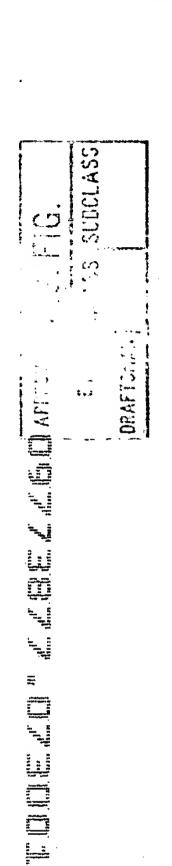
1690 1700

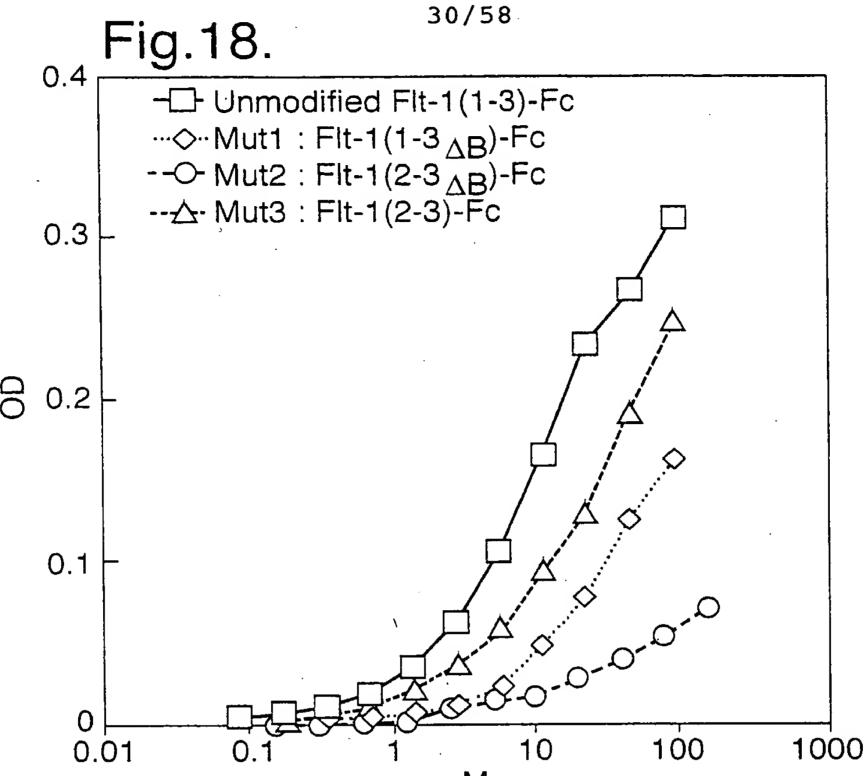
CTC TCC CTG TCT CCG GGT AAA TGA GAG AGG GAC AGA GGC CCA TTT ACT Leu Ser Leu Ser Pro Gly Lys ***>

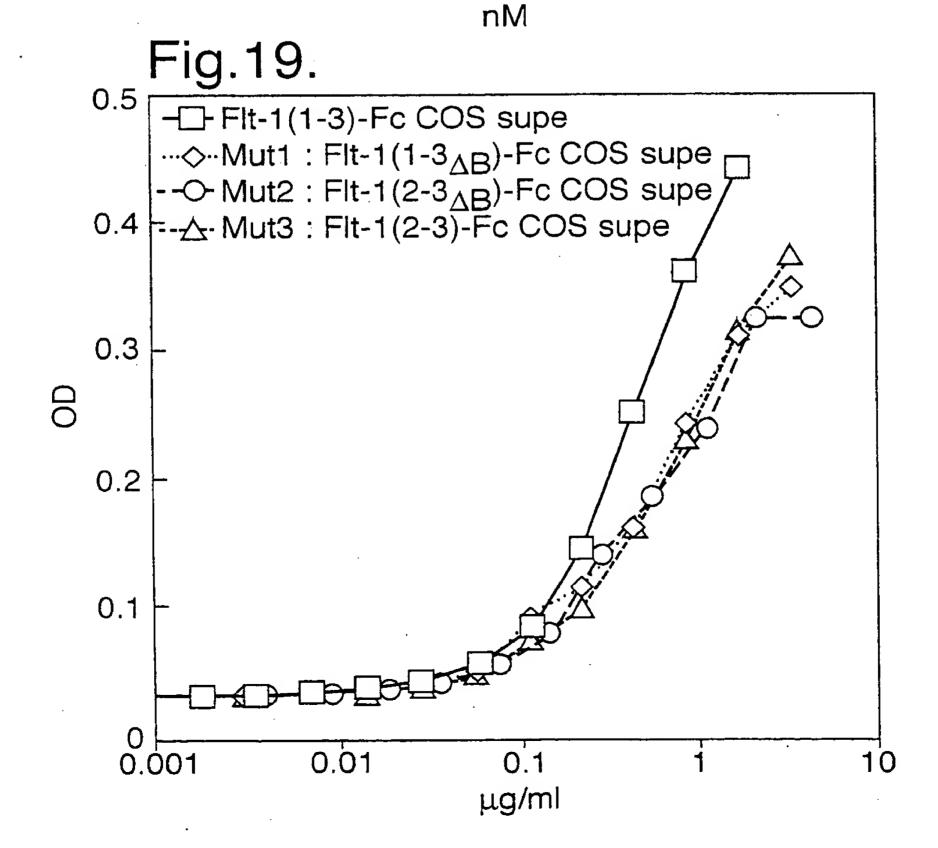


Fig.17.

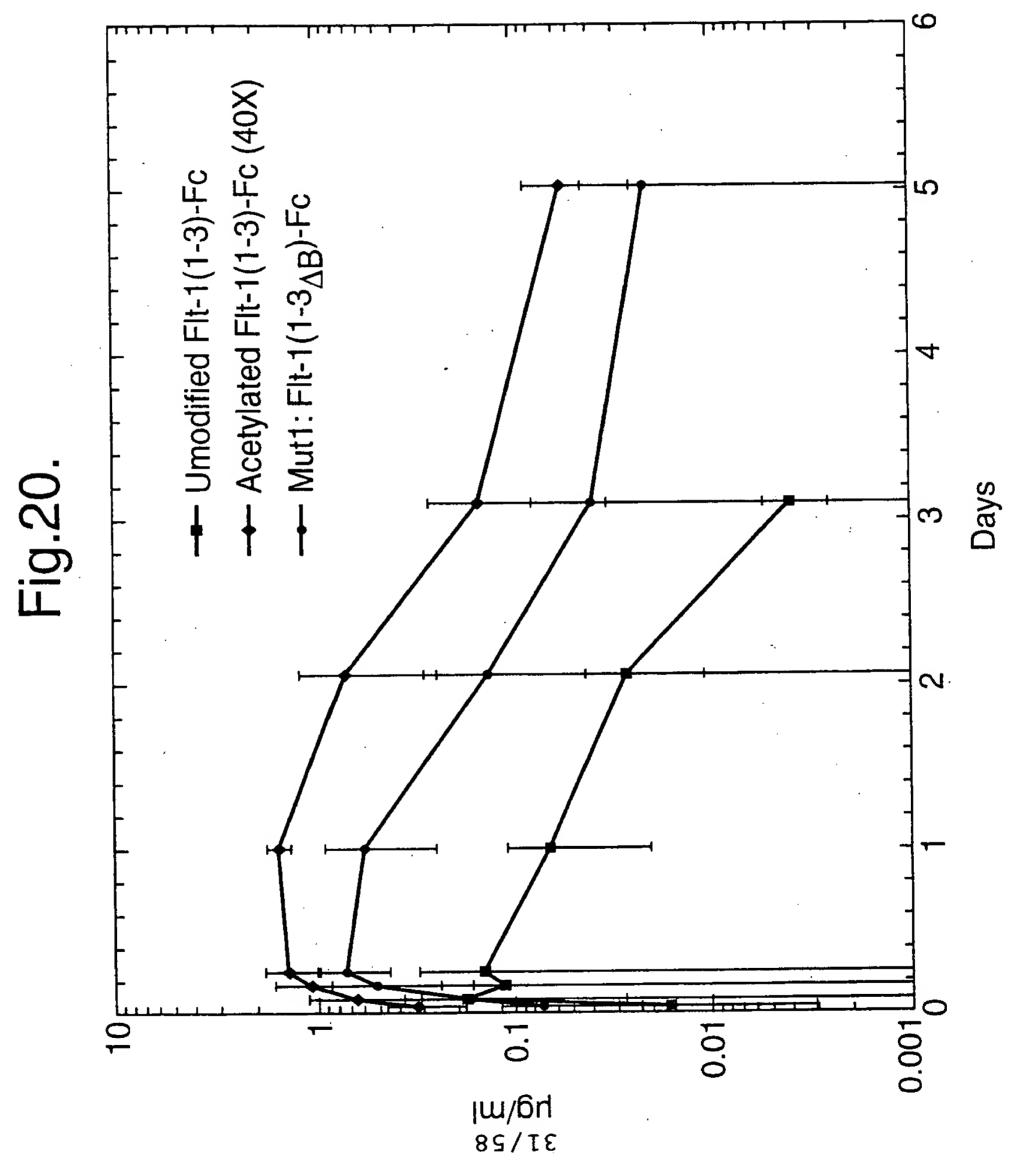
















	•						
Fig	.21A.			>EcoRI	_site		
10	20	30	40	50	60	70	8
CTTGGGCTGCA							
CGAACCCGACGT	CCAGCTAGCT	GAGATCTCCT	'AGCTAGGGGC	CCGCTCGAGC	CTTAAGCGTTG	etggtaccag M V	TCGAT S Y
					_	1	4
					>BspEI_bric	dae	
			,			age	
90	100	110	120	130	140	150	16
GACACCGGGGT	001001010	GCGCTGCTCA	.001010100	TCTCACAGG!		GAGGTAGACC CTCCATCTCC	
CCTGTGGCCCCA V G T G	GGACGACACG 'LLC	A L L			S S>	CICCAICIGG	mn.G
		FLT1 SS_			>		
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TCTACATGTCAC	TTTAGGGGCT	TTAATATGT	GTACTGACTT	CCTTCCCTCG		•	ACGTC IGCAG
AGATGTACAGTG TCTACATGTCAC	AAATCCCCGA	AATTATACA( TTAATATGT(	CATGACTGAA GTACTGACTT M T E	GAAGGGAGC CCTTCCCTCG GRE	TCGTCATTCCC AGCAGTAAGGG L V I P	TGCCGGGTT? ACGGCCCAAT	ACGTC IGCAG T S
AGATGTACAGTG TCTACATGTCAC	SAAATCCCCGA TTTAGGGGCT	AATTATACA( TTAATATGT(	CATGACTGAA GTACTGACTT M T E	GAAGGGAGC' CCTTCCCTCG	TCGTCATTCCC AGCAGTAAGGG L V I P	TGCCGGGTT? ACGGCCCAAT	ACGTC IGCAG T S
AGATGTACAGTG TCTACATGTCAC	SAAATCCCCGA CTTTAGGGGCT E I P E	AATTATACA( TTAATATGT( I I H	CATGACTGAA GTACTGACTT M T E	GGAAGGGAGC CCTTCCCTCG G R E	TCGTCATTCCC AGCAGTAAGGG L V I P	TGCCGGGTT? ACGGCCCAAT	ACGTC. FGCAG T S 5
AGATGTACAGTG TCTACATGTCAC E M Y S 250 AACATCACTGTT	AAATCCCCGA TTTAGGGGCT E I P E 260	AATTATACAC TTAATATGTC I I H 270 AGTTTCCAC	CATGACTGAAG STACTGACTTO M T EHFLT1 D2 280 TTGACACTTT	GAAGGGAGC CCTTCCCTCG G R E 290 GATCCCTGAT	TCGTCATTCCC AGCAGTAAGGG L V I P  300 GGAAAACGCAT	TGCCGGGTTA ACGGCCCAAT C R V 310	ACGTC. FGCAG T S 5
AGATGTACAGTG TCTACATGTCAC E M Y S  250 AACATCACTGTTACTTACTACTACTACTACTACTACTACTACTACTACTA	AAATCCCCGA TTTAGGGGCT E I P E 260 TACTTTAAAAA	AATTATACAC TTAATATGTC I I H 270 AGTTTCCAC	CATGACTGAAG GTACTGACTT M T EHFLT1 D2 280 TTGACACTTT AACTGTGAAA	GAAGGGAGC CCTTCCCTCG G R E 290 GATCCCTGAT CTAGGGACTA	TCGTCATTCCC AGCAGTAAGGG L V I P  300 GGAAAACGCAT	TGCCGGGTTA ACGGCCCAAT C R V 310 AATCTGGGAC	ACGTC T S 5 2 CAGTA
AGATGTACAGTG TCTACATGTCAC E M Y S  250 AACATCACTGTT	AAATCCCCGA TTTAGGGGCT E I P E 260 TACTTTAAAAA	AATTATACAC TTAATATGTC I I H 270 AGTTTCCAC	CATGACTGAAG STACTGACTTO M T EHFLT1 D2 280 TTGACACTTT	GAAGGGAGC CCTTCCCTCG G R E 290 GATCCCTGAT CTAGGGACTA	TCGTCATTCCC AGCAGTAAGGG L V I P  300 GGAAAACGCAT	TGCCGGGTTA ACGGCCCAAT C R V 310 AATCTGGGAC	ACGTC FGCAG T S 5 CAGTA GTCAT
AGATGTACAGTG TCTACATGTCAC E M Y S  250 AACATCACTGTTACTTACTACTACTACTACTACTACTACTACTACTACTA	AAATCCCCGA TTTAGGGGCT E I P E 260 TACTTTAAAAA	AATTATACAC TTAATATGTC I I H 270 AGTTTCCAC	CATGACTGAAG GTACTGACTT M T EHFLT1 D2 280 TTGACACTTT AACTGTGAAA	GAAGGGAGC CCTTCCCTCG G R E 290 GATCCCTGAT CTAGGGACTA I P D	TCGTCATTCCC AGCAGTAAGGG L V I P  300 GGAAAACGCAT	TGCCGGGTTA ACGGCCCAAT C R V 310 AATCTGGGAC	ACGTC T S 5 CAGTA GTCAT
AGATGTACAGTG TCTACATGTCAC E M Y S  250 AACATCACTGTT TTGTAGTGACAA N I T V	AAATCCCCGA TTTAGGGGCT E I P E 260 TACTTTAAAAA ATGAAATTTTT T L K	AATTATACAC TTAATATGTC I I H  270 AGTTTCCACC TCAAAGGTG	CATGACTGAAG GTACTGACTT M T EHFLT1 D2 280 TTGACACTTT AACTGTGAAA L D T LHFLT1 D2	GAAGGGAGC CCTTCCCTCG G R E 290 GATCCCTGAT CTAGGGACTA I P D	TCGTCATTCCC AGCAGTAAGGG L V I P  300 GGAAAACGCAT CCTTTTGCGTA	TGCCGGGTTA ACGGCCCAAT C R V  310 AATCTGGGAC TTAGACCCTC	ACGTC FGCAG T S 5 CAGTA GTCAT
AGATGTACAGTG TCTACATGTCAC E M Y S  250 AACATCACTGTT TTGTAGTGACAA N I T V	AAATCCCCGA TTTAGGGGCT E I P E 260 TACTTTAAAAA ATGAAATTTTT T L K	AATTATACAC TTAATATGTC I I H  270 AGTTTCCAC TCAAAGGTG K F P	CATGACTGAAG GTACTGACTTGACTTGACTTTACTGACACTTTGACACTTTGACACTTTCACACTTTCACACTTTCACACTGAAAALDTL	GAAGGGAGC CCTTCCCTCG G R E 290 GATCCCTGAT CTAGGGACTA I P D	TCGTCATTCCC AGCAGTAAGGG L V I P  300 GGAAAACGCAT CCTTTTGCGTA G K R I	TGCCGGGTTA ACGGCCAAT C R V  310 AATCTGGGAC TTAGACCCTC I W D	ACGTC FGCAG T S 5 CAGTA GTCAT S
AGATGTACAGTG TCTACATGTCAC E M Y S 250 AACATCACTGTT TTGTAGTGACAA N I T V 330 AGGGCTTCATCAC	AAATCCCCGA TTTAGGGGCT E I P E  260 TACTTTAAAAA ATGAAATTTT T L K  340 TATCAAATGCA	AATTATACAC TTAATATGTC I I H  270 AGTTTCCAC TCAAAGGTG K F P  350 ACGTACAAA	CATGACTGAAG GTACTGACTT M T E HFLT1 D2  280 TTGACACTTT AACTGTGAAA L D T L HFLT1 D2  360 GAAATAGGGC	GAAGGGAGC CCTTCCCTCG G R E  290 GATCCCTGAT CTAGGGACTA I P D  370 TTCTGACCTG	TCGTCATTCCC AGCAGTAAGGG L V I P  300 GGAAAACGCAT CCTTTTGCGTA G K R I  380 TGAAGCAACAC	TGCCGGGTTA ACGGCCAAT C R V  310 AATCTGGGAC TTAGACCCTC I W D  390 ATCAATGGGC	ACGTC FGCAG T S 5 CAGTA GTCAT S
AGATGTACAGTG TCTACATGTCAC E M Y S  250 AACATCACTGTT TTGTAGTGACAM N I T V  330 AGGGCTTCATCAC CCCGAAGTAGT	AAATCCCCGA TTTAGGGGCT E I P E  260 TACTTTAAAAA ATGAAATTTT T L K  340 TATCAAATGCA	AATTATACAC TTAATATGTC I I H  270 AGTTTCCAC TCAAAGGTG K F P  350 ACGTACAAA	CATGACTGAAG GTACTGACTT M T E HFLT1 D2  280 TTGACACTTT AACTGTGAAA L D T L HFLT1 D2  360 GAAATAGGGC	GAAGGGAGC CCTTCCCTCG G R E  290 GATCCCTGAT CTAGGGACTA I P D  370 TTCTGACCTG	TCGTCATTCCC AGCAGTAAGGG L V I P  300 GGAAAACGCAT CCTTTTGCGTA G K R I  380 TGAAGCAACAC	TGCCGGGTTA ACGGCCAAT C R V  310 AATCTGGGAC TTAGACCCTC I W D  390 ETCAATGGGC	ACGTC FGCAG T S 5 CAGTA GTCAT S
AGATGTACAGTG TCTACATGTCAC E M Y S  250 AACATCACTGTT TTGTAGTGACAM N I T V  330 AGGGCTTCATCAC CCCGAAGTAGT	AAATCCCCGA TTTAGGGGCT E I P E  260 TACTTTAAAAA ATGAAATTTT T L K  340 TATCAAATGCA	AATTATACAC TTAATATGTC I I H  270 AGTTTCCAC TCAAAGGTG K F P  350 AACGTACAAA	CATGACTGAAG GTACTGACTT M T E HFLT1 D2  280 TTGACACTTT AACTGTGAAA L D T L HFLT1 D2  360 GAAATAGGGC CTTTATCCCG E I G	290 GATCCCTGAT CTAGGGACTA I P D  370 TTCTGACCTG AAGACTGGAC L L T C	TCGTCATTCCC AGCAGTAAGGG L V I P  300 GGAAAACGCAT CCTTTTGCGTA G K R I  380 TGAAGCAACAC ACTTCGTTGTC E A T	TGCCGGGTTA ACGGCCCAAT C R V  310 AATCTGGGAC TTAGACCCTC I W D  390 ETCAATGGGC CAGTTACCCG	ACGTC. FGCAG T S S CAGTA GTCAT S ATTTC
AGATGTACAGTG TCTACATGTCAC E M Y S  AACATCACTGTT TTGTAGTGACAM N I T V  330 AGGGCTTCATCAC CCCGAAGTAGTM	AAATCCCCGA TTTAGGGGCT E I P E  260 TACTTTAAAAA ATGAAATTTT T L K  340 TATCAAATGCA	AATTATACAC TTAATATGTC I I H  270 AGTTTCCAC TCAAAGGTG K F P  350 AACGTACAAA	CATGACTGAAG GTACTGACTT M T E HFLT1 D2  280 TTGACACTTT AACTGTGAAA L D T L HFLT1 D2  360 GAAATAGGGC CTTTATCCCG E I G	290 GATCCCTGAT CTAGGGACTA I P D  370 TTCTGACCTG AAGACTGGAC L L T C	TCGTCATTCCC AGCAGTAAGGG L V I P  300 GGAAAACGCAT CCTTTTGCGTA G K R I  380 TGAAGCAACAC	TGCCGGGTTA ACGGCCCAAT C R V  310 AATCTGGGAC TTAGACCCTC I W D  390 ETCAATGGGC CAGTTACCCG	T S  CAGTA GTCAT S  ATTTC TAAAC H L
AGATGTACAGTG TCTACATGTCAC E M Y S  AACATCACTGTT TTGTAGTGACAA N I T V  330 AGGGCTTCATCAC CCCGAAGTAGTA CCCGAAGTAGTAC CCCGAAGTAC CCCGAAGTAC CCCGAAGTAC CCCGAAGTAC CCCGAAGTAC CCCGAAGTAC CCCGAAGTAC CCCGAAGTAC CCCCGAAGTAC CCCGAAGTAC CCCGAAGTAC CCCCGAAGTAC CCCCGAAGTAC CCCGAAGTAC CCCCGAAGTAC CCCCGAAC CCCCGAAGTAC CCCCGAAC CCCCCCCCCC	260 PACTITAGEGECT E I P E  260 PACTITAAAAA ATGAAATTTT T L K  340 PATCAAATGCA ATAGTTTACGT I S N A	AATTATACAC TTAATATGTC TTAATATGTC I I H  270 AGTTTCCAC TCAAAGGTG K F P  350 AACGTACAAA TTGCATGTTT T Y K	CATGACTGAAG GTACTGACTT M T E HFLT1 D2  280 TTGACACTTT AACTGTGAAA L D T L HFLT1 D2  360 GAAATAGGGC CTTTATCCCG E I G HFLT1 D2  440	290 GATCCCTGAT CTAGGGACTA I P D  370 TTCTGACCTG AAGACTGGAC L L T C	TCGTCATTCCC AGCAGTAAGGG L V I P  300 GGAAAACGCAT CCTTTTGCGTA G K R I  380 TGAAGCAACAC ACTTCGTTGTC E A T	TGCCGGGTTA ACGGCCAAT C R V  310 AATCTGGGAC TTAGACCCTC I W D  390 TCAATGGGC AGTTACCCG V N G	ACGTC. IGCAG T S S CAGTA GTCAT S ATTTC TAAAC H L
AGATGTACAGTG TCTACATGTCAC E M Y S  250 AACATCACTGTT TTGTAGTGACAF N I T V  330 AGGGCTTCATCAT CCCGAAGTAGTF CCCCGAAGTAGTF CCCCCAAGTAGTT CCCCCAAGTAGTT CCCCCAAGTAGTT CCCCCAAGTAGTT CCCCCAAGTAGT	260 PACTITAGEGECT E I P E  260 PACTITAAAAA ATGAAATTTT T L K  340 PATCAAATGCA ATAGTTTACGT I S N A  420 CTCACACATCC	AATTATACAC TTAATATGTC TTAATATGTC I I H  270 AGTTTCCAC TCAAAGGTG K F P  350 ACGTACAAA TGCATGTTT T Y K  430 ACAAACCAA	CATGACTGAAG GTACTGACTT M T E HFLT1 D2  280 TTGACACTTT AACTGTGAAA L D T L HFLT1 D2  360 GAAATAGGGC CTTTATCCCG E I G HFLT1 D2  440 TACAATCATA	290 GATCCCTGAT CTAGGGACTA I P D  370 TTCTGACCTG AAGACTGGAC L L T C	TCGTCATTCCC AGCAGTAAGGG L V I P  300 GGAAAACGCAT CCTTTTGCGTA G K R I  380 FGAAGCAACAC ACTTCGTTGTC E A T  460 CTGAGTCCGTC	TGCCGGGTTA ACGGCCAAT C R V  310 AATCTGGGAC TTAGACCCTC I W D  390 ATCAATGGGC V N G  470 ICATGGAATT	ACGTC. IGCAG T S S CAGTA GTCAT S ATTTC TAAAC H L
AGATGTACAGTG TCTACATGTCAC TCTACATGTCAC E M Y S  250 AACATCACTGTT TTGTAGTGACAA N I T V  330 AGGGCTTCATCAC CCCGAAGTAGTA CCCGAAGTAGTAC CCCGAAGTAGTAC CTCTGTTTGATAC TCTGTTTGATAC	260 PACTITAGEGECT E I P E  260 PACTITAAAAA  TGAAATTTT T L K  340 PATCAAATGCA  ATAGTTTACGT I S N A  420 CTCACACATCC GAGTGTGTAGC	AATTATACAC TTAATATGTC TTAATATGTC I I H  270 AGTTTCCAC TCAAAGGTG K F P  350 ACGTACAAA TTGCATGTTT T Y K  430 EACAAACCAA CTGTTTGGTT	CATGACTGAAG GTACTGACTTO M T E HFLT1 D2  280 TTGACACTTTO AACTGTGAAA L D T L HFLT1 D2  360 GAAATAGGGC CTTTATCCCG E I G HFLT1 D2  440 TACAATCATA CATGTTAGTAT	290 GATCCCTGAT CTAGGGACTA I P D  370 TTCTGACCTG AAGACTGGAC L L T C  450 CGATGTGGTTC CTACCACCAAC	TCGTCATTCCC AGCAGTAAGGG L V I P  300 GGAAAACGCAT CCTTTTGCGTA G K R I  380 FGAAGCAACAC ACTTCGTTGTC E A T  460 CTGAGTCCGTC	TGCCGGGTTA ACGGCCAAT C R V  310 AATCTGGGAC TTAGACCCTC I W D  390 ATCAATGGGC V N G  470 ICATGGAATT	ACGTC. IGCAG T S CAGTA GTCAT S ATTTC TAAAC H L
AGATGTACAGTG TCTACATGTCAC E M Y S  250 AACATCACTGTT TTGTAGTGACAF N I T V  330 AGGGCTTCATCAC CCCGAAGTAGTE C G F I	260 PACTITAGEGECT E I P E  260 PACTITAAAAA ATGAAATTTT T L K  340 PATCAAATGCA ATAGTTTACGT I S N A  420 CTCACACATCC GAGTGTGTAGC	AATTATACAC TTAATATGTC TTAATATGTC I I H  270 AGTTTCCAC TCAAAGGTG K F P  350 ACGTACAAA TTGCATGTTT T Y K  430 EACAAACCAA CTGTTTGGTT R Q T N	CATGACTGAAG GTACTGACTTO M T E HFLT1 D2  280 TTGACACTTTO AACTGTGAAA L D T L HFLT1 D2  360 GAAATAGGGC CTTTATCCCG E I G HFLT1 D2  440 TACAATCATA CATGTTAGTAT	290 GATCCCTGAT CTAGGGACTA I P D  370 TTCTGACCTG AAGACTGGAC L L T C  450 CGATGTGGTTC CTACACCAAC CTACACCAAC	TCGTCATTCCC AGCAGTAAGGG L V I P  300 GGAAAACGCAT CCTTTTGCGTA G K R I  380 FTGAAGCAACAC ACTTCGTTGTC E A T  460 CTGAGTCCGTCC GACTCAGGCAG	TGCCGGGTTA ACGGCCAAT C R V  310 AATCTGGGAC TTAGACCCTC I W D  390 ATCAATGGGC V N G  470 ICATGGAATT	ACGTC. IGCAG T S CAGTA GTCAT S ATTTG TAAAC H L

_HFLK1 D3_____>



ORAFISH

33/58

Fig.21B.

1	19.2	IJ.						
490	50			520			550	
CTGTTGGAGA			-					
SACAACCTCTT	rttcgaaca	GAATTTAAC			SATTTACACC	CCTAACTGAA		PATGGGA
S V G E	K L V	LNC	A T	R T E	L N V	GIDF	NWE	Y P>
				-				164
				HFLK1 D3	<u></u> <u>-</u>	<del></del>	<del> </del>	>
		_		<b></b>	63.0	600	63.0	
570	58			600			630	640
TCTTCGAAGC								
AGAAGCTTCG								AAAACIC F L S>
SSKI	H Q H	KKL	VNR	D L K	T Q S	G S E		r <u>1</u> 32
				HFLK1 D3_				>
	<del></del>		<del></del>	THE THE TOT		<u></u>		
650	66	0 (	570	680	690	700	710	720
CACCTTAACT		-						
CACCTTAACT/ GTGGAATTGA!								
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				HFLK1 D3				>
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,				<b>5</b> –				
730	74		750 İ	760	770	780	790	800
AGAACAGCAC	ል <b>ጥጥ</b> ርጥር ልር	בבידיר באיזיק:	AAAGGGG	CCGGGCGAC	AAAACTCACA	CATGCCCAC	CTGCCCAGC	ACCTGAA
	_HFLKI D3		G	P G> > D	к т н	T C P	P C P A	A P E>
						FCAC1 (A	)	2 *
810	82	20	830	840	850	860	870	880
CTCCTGGGGG								AGGTCAC
GAGGACCCCC								
	G P S	V F L		ркрк		M I S	R T P	E V T
пп	G I D	V 1 2						2'
		•		FCΔC1(A)				
					·			
890	ı. 9(	00	910	920	930	940	950	960
ATGCGTGGTG				GAGGTCAAGT	TCAACTGGT	ACGTGGACGG	CGTGGAGGT	CATAATG
TACGCACCAC								
C V V	V D V	S H E				YVDG		H N>
	, , ,							297
				_FCΔC1 (A)_	<u></u>			
970	9!	В0	990	1000	1010	1020	1030	1040
CCAAGACAAA							•	AGGACTGG
GGTTCTGTTT								
A K T K		E E O	Y N S		v v s	V L T		Q D W>
A 1 1 1		x	<b>~</b>		-	_		32
				_FC∆C1 (A)_				
				\- '- ' -				· — <del> </del>



Fig.21C.

		10	50		10	60			10	70		10	80		1	090			110	0		1:	110			112	20
CTG.	AAT	GG	CAA	GGAC	TAC	'AAC	TG	CA	AGG'	TCTC	CAA	CAA	AGCC	CTC	CC	AGC	CCC	CAT	'CGA	GAA	AAC	CA.	rch	CCA	AAC	CC.	A.A.
GAC	TTA	CC	GTT	CCTC	ATC	TT	CAC	GT'	TCC.	AGAC	GTI	GTT	I'CGC	GAG	GG'	TCG	GGG	GTA	.GCT	CTT	TTC	GT	AGA	<b>3GT</b>	TTC	GG:	$\Gamma T$
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Fig.22	∠ <b>A</b> .		•	>EcoRI_	_site		
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170 180 GAGATGTACAGTGAAATCO	•						
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			IG DOMAIN				
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N I I V I D							84
		FLT1	IG DOMAIN	2			
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330 34 AGGGCTTCATCATATCAA		350 TACAAAGA					
TCCCGAAGTAGTATAGTT	TACGTTGC	ATGTTTCT		GACTGGACA		AGTTACCCGT	
	it 3 m	YKE	I G L	L T C	EAT	N G H	
K G F I I S	N A T	• • • -					
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410 42	0 CATCGACA	430 AACCAATA	IG DOMAIN  440  CAATCATAGA	450 TATCCAGCT	460 GTTGCCCAGG	470 AAGTCGCTGG	48 AGCTG
410 42 TAAGACAAACTATCTCACA ATTCTGTTTGATAGAGTGT	0 CATCGACA GTAGCTGT	430 AACCAATA	IG DOMAIN  440  CAATCATAGA  GTTAGTATC	450 TATCCAGCT	460 GTTGCCCAGG	470 AAGTCGCTGG	48 AGCTG
410 42 TAAGACAAACTATCTCACA ATTCTGTTTGATAGAGTGT K T N Y L T	0 CATCGACA GTAGCTGT H R C	430 AACCAATA TTTGGTTAT	IG DOMAIN  440  CAATCATAGA  GTTAGTATCAT  T I I	450 TATCCAGCT ATAGGTCGA	460 GTTGCCCAGG	470 AAGTCGCTGG	AGCTG
410 42 PAAGACAAACTATCTCACA ATTCTGTTTGATAGAGTGT	0 CATCGACA GTAGCTGT H R C	430 AACCAATA TTTGGTTAT	IG DOMAIN  440  CAATCATAGA  GTTAGTATCAT  T I I	450 TATCCAGCT ATAGGTCGA >> >	460 GTTGCCCAGG	470 AAGTCGCTGG ITCAGCGACC	48 AGCTG TCGAC
410 42 TAAGACAAACTATCTCACA ATTCTGTTTGATAGAGTGT K T N Y L T	0 CATCGACA GTAGCTGT H R C	430 AACCAATA TTTGGTTAT	IG DOMAIN  440  CAATCATAGA  GTTAGTATCAT  T I I	450 TATCCAGCT ATAGGTCGA > _> I Q I	460 GTTGCCCAGG ACAACGGGTCC	470 AAGTCGCTGG ITCAGCGACC K S L	480 AGCTGO TCGACO E L>



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Fig.22B.

490	500	510	520	530	540	550	560
rggtaggggagaag							
CCATCCCCTCTTC	GACCAGGAGT						
VGEK	L V L	N C T V	WAI	E F N S	GVTI	FDWD	Y P>
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		VEGFR3	(FLT4) IC	G DOMAIN 3_			>
			600	610	<b>600</b>	<b>620</b>	640
				610			640
GGAAGCAGGCAGA	•						
CCTTCGTCCGTCT			E R R				AGGACIG I L T>
GKQAE	RGK	WVP	EKK	SQQI	n i E	ь з з .	19
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		FCΔ	C1 - A AL	LOTYPE			

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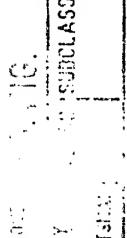
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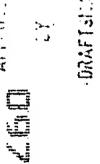


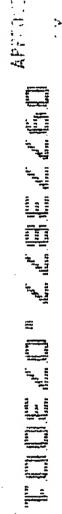
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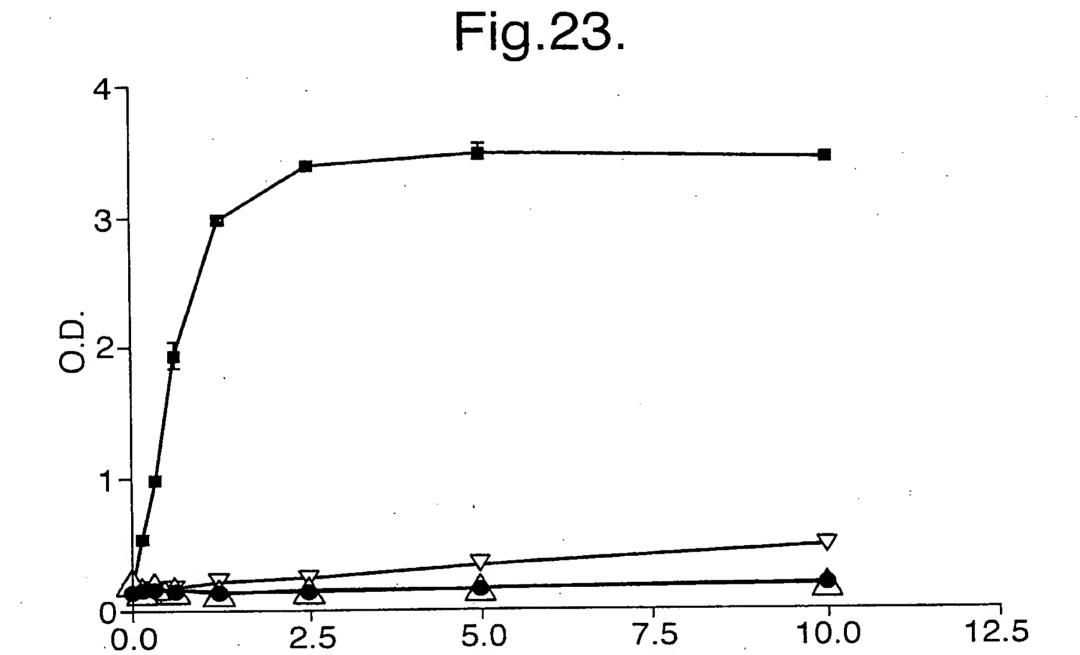
# Fig.22C.

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CCGAAGATAGG G F Y P	STCGCTG S D	TAGC I	GGCA A V	CCTY E F	CACC W CAC1	E - A >1	S I A AL:	TACC N G	CGTC Q TPE	P GGC	E	TGT N	TGA N	TGT Y	TCT K	GGT T	rGC(	P 13	GG P> 40
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CCGAAGATAGG G F Y P 1290 GCTGGACTCCG CGACCTGAGGC	STCGCTG S D 1300 ACGGCTC	TAGC	13 TTCC	CCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTC	CACC W CAC1	ETCT E  - A  >T  132 CAAC	S I A AL COMPANY COMPA	TACC N G	CGTC Q PE	CAA	E GAGO	N N SAGG	TGA N	TGT Y	TCT K	GGT T	GC( T	P 13	60 40 60
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1290 GCTGGACTCCG CGACCTGAGGC	1300 ACGGCTC IGCCGAG D G S	TAGC I CTTC GAAG F	13 TTCC AAGG	CCTC E F  10 CTCT AGA L	CACC W CAC1 ATAC TATC	ETCT E - A - A - 132 CAAC CGTTC K	S I A AL COTO COTO COTO COTO COTO A AL A AL A	TACC N G LOTY ACCC TGGC	CGTC Q PE	CAA(CTT)	GAGO CTCO	N 340 CAGG	TGA N TGG ACC W	TGT Y CAG GTC Q	TCT K	GGT T GGGG GGGC G	GCC T GAAC CTTC N	P P CGTC CGTC CGTC V	GC P> 40 60 TT
1290 GCTGGACTCCG CGACCTGAGGC L D S	1300 ACGGCTC TGCCGAG D G S	TAGC I CTTC GAAG F	13 TTCC AAGG F	CCTC E F  10 TCT AGA LF	CACC W CACC ATAG TATC Y CACC	ETCT E  - A  >1  132 CAAC CGTTC K	S I A AL COTO COTO COTO COTO COTO COTO COTO COT	TACC N G LOTY ACCC TGGC	CGTC Q PE_ 1330 TGGA ACCT V I	CAA(CTT)	GAGO CTCO	N 340 CAGG STCC R	TGA N TGG ACC W	TGT Y CAG GTC Q	TCT K 135 CAG CGTC Q	GGT T GGGC GGGC G	GCC T GAAC CTTC N	P  13  CGTC  GCAC  V  DtI_ 14	60 40 60 377 6AZ 140
1290 GCTGGACTCCG CGACCTGAGGC L D S 1370 CATGCTCCGTG	1300 ACGGCTC TGCCGAG D G S  1380 ATGCATG	TAGC I CTTC GAAG F	13 TTCC AAGG F	CCTC E F  10 CTCT AGA L	CACC W CACC ATAG TATC Y S CACC	ETCT E  - A  >1  132 CAAC CGTTC K	S I A AL COTC CGAG CGAG A AL COCACO	TACC N G LOTY ACCC TGGC T LOTY	CGTC Q PE_ 1330 ACCT V I PE_ 1410 AAGA	CAA(CAA(CAA(CAA(CAA(CAA(CAA(CAA(CAA(CAA	GAGO CTCO S	340 CAGG STCC R	TGA N TGG ACC W	TGT Y CAG GTC Q	TCT K 135 CAG CGTC Q	GGT T GGGC GGGC GGGC GGGC GGGC GGGC GGG	GCC T TTC N >NC TTA	13 CGTC SCAC V	GC P> 40 60 ETT AAA P 40 40 40 CGC
1290 CCTGGACTCCG CGACCTGAGGC L D S 1370 CATGCTCCGTG	1300 ACGGCTC IGCCGAG D G S  1380 ATGCATG TACGTAC	TAGC I CTTC GAAG F	13 TTCC AAGG F	CCTC E F  10 CTCT AGA L	CACC W CACC ATAG TATC Y S CACC	ETCT E  - A  >1  132 CAAC CGTTC K	S I A AL COTO CGAG CGAG CGAG CGTG	TACC N G LOTY ACCC TGGC T LOTY	CGTC Q PE_ 1330 ACCT V I PE_ 1410 AAGA	CAA CAA CTT K	GAGO CTCO S TCTO	340 CAGG STCC R	TGA N TGG ACC W	TGT Y CAG GTC Q	TCT K  135 CAG CGTC Q	GGT T GGGC GGGC GGGC GGGC GGGC GGGC GGG	GCC T T SAA( CTTC N >NC	13 CGTC SCAC V	GG P> 40 60 TT AA F 40 Si
1290 CGTGGACTCCG CGACCTGAGGC L D S 1370 CATGCTCCGTG	1300 ACGGCTC IGCCGAG D G S  1380 ATGCATG TACGTAC	TAGC I CTTC GAAG F AGGC TCCG	13 TTCC AAGG F	CCTC E  10 TCT AGA L  90 CAC	CACCI W CACI ATAG TATCI Y CACI CACI	ETCT E  - A  >T  132 CAAC CGTTC  K  140 CACTA	S I ALI	TACC N G LOTY T LOTY GCAC	CGTC Q TPE	CAA CAA CTT CTT	GAGO CTCO S TCTO	AGG R L420 CCCI	TGA	TGT Y CAG GTC Q	TCT K  135 CAG CGTC Q	GGT T GGGC GGGC GGGC GGGC GGGC GGGC GGG	GCC T TTC N >NC TTA	13 CGTC SCAC V	GC P> 40 60 ETT AAA P 40 40 40 CGC









- Flt1D2Flk1D3.FcdeltaC1(a)
- △FIt1D2VEGFR3D3.FcdeltaC1(a)

[Modified Flt Receptor] (nM)

- ♥ TIE2-Fc
- Flt1 (1-3)-Fc



Fig.24A.

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GGG	CTT	TAA	TAT	GTG	TAC	TGA	CTT								_				
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GGA	TIG	TAG	TGA	CAA	TGA	AAT	TTT	TTC	AAA	GGT	GAA	CIG	TGA	AAC	TAG	GGA	CTA	CCT	TTT
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CCC	אנחא	አጥ		GAC	Σرتب						ATA	TCA	raa .	GCA	ACG	TAC	AAA	GAA	ATA
GCG	ጥልጥ	TAG	ACC	CIG	TCA	TCT	TTC	CCG	AAG	TAG	TAT	AGI	TTA	CGI	' TGC	ATG	TTT	CIT	TAT
Ð	Τ.	Ŧ	<b>TAT</b>	ת	S	R	K	G	F	I	I	S	N	A	${f T}$	Y	K		I>
81_				85			h	FLT1	IG	DOMA	IN 2	2		95		<u></u>		·	_100>
									220			-	40			350			360
		3	10			320			330			-	*			*			360 *
	~~~	~~~	* *~~	, 117-117	ת תים	י. ברא	አ ጉ	CITY.	 דיבבי	, GG:	CAT	י ייייני		r AAG	AC.	A AAC	LAT	CIC	ACA
~~	CLI	CIG	י חרבי	. IGI	للملك	CGT	TGT	CAG	TTA		GTA	AA A	ATA	TTC	TG	PTT T	ATA	GAG	TGT
G	τ.	Τ.	ጥ	С	E	A	${f T}$	V	N	G	H	L	Y	K	${f T}$	N	Y	L	T>
101				105)		h	FLT1	IG	DOM	IN 2	2		115	5				120>
		. 3	370			380			390)		4	400			410			420
		.	*	<u>.</u>		*		~	د	. Caller	n (~Tr	ב ארב	* ኮ ~~	∡ . ⊔\	יער) יו	ני בולבי ות ע	7 <u>7</u> 114	የ ርልን ባ	A CTA
CAT	CGA	CAZ	A ACC	I'AA :	, ACA	OTA A	ATA :	GAT	י פור	ימין י	7 CD(ישרים. מאר ב	A GCG	C AG	A Cab	A CC	TAT 1	A CIT	A CTA C GAT
		GIN	_	TIP N	T TG1	. TAC	I.	D>			. (36)	- 1 ·		عبده ب					<u>-</u>
H -121	R	Q hi	ጥ ተም1	IGI	_		_												
						,			_ v	V	L	S	P	S	Н	G	Ţ	E	
										_		1		TA 12	~~~	NT 2			140



Fig.24B

		ı	15	<i>ع</i> ٠٠		.													
		43	0 *		4	40 *			450 *			46	50 *			.70 *			480 *
AGA	CAA	CCT	CTT	AAG TTC K	GAA	CAG .	TAA	TTA	ACA	TGT	CGT	TCT	TGA	CTT	GAT	TTA	CAC	CCC	AAT
141_	<u>.</u>			_145_			h	FLK1	IG	DOMA	IN 3	3		_155_		_			160>
		49	90 *		5	000 *										530 *			
CTG D	AAG F	TTG N	ACC W	GAA CTT E _165_	ATG Y	GGA P	AGA S	AGC S	TTC	GTA H	GTC Q	GTA H	TTC K	TTT K	GAA L	CAT V	TTG N	GCT R	CTG D>
									-			5	80		5	590			600
GAT L	TTT	TGG T	GIC	TCT AGA S 185	CCC	TCA S	CIC	TAC M	TTC K	AAA TTT K	AAA F	TTG AAC L	AGC TCG S	TGG T	TTA AAT L	ACT TGA T	TAT	GAT CTA D	CCA
			10			520			630				40			650			660
CAT V	TGG T	GCC R	TCA S	GAC CTG D	GII	CCT	AAC L	ATG Y	TGG T	ACA C	CGT A	A CGI	'AGG S	TCA S	CCC	GAC L	TAC M	ACC TGG T	AAG TTC
			70	-		680			690			7	700			710			
TIC	N N	TOG S	ACA TGT	TTT AAA F	GTC CAG V	AGG TCC R	GTC CAG V	CAT GTA H	GAA CTT E	AAG TTC K>	GAC	AAA	ACI	CAC	ACA	TGC	CCA GGT	, eec	TGC
221	· <u> </u>	· .	_hFI	Kl I	G DO	MAIN	3			_231	D					C A			C> _240>
		7	730			740			750 *				760 *			770			780
GGI P	r CGT A	r GGZ	A CM	CAG	GAC L	CCC G	GGA CCI G	CCG GGC	TCA AGI S	GTC CAC V	TTC AAC F	CTY GAG L	TTC AAC F	200 GGG P	CCA GGT P	AAA TTT K	P GGC	TTC K	GAC CTG D>
			790			800							820			830			840
TG(GA(L	AT E M	AT C I	DOA E	GCC R	TGG T	GGA P	CTC E	CAC V	TG.	A TGO T ACO C	C GT G CA V	G GTY C CA	C CAC V	GAC CIC D	OTO CAO V	TC S	VID E H	GAA G CTT E> 280:
			850			860				0									900
CT	G GG	A CT	C CA	G TT	TTY	G TTC	TG(TA C	C GIV	G GA	G CC	G CA	C CT	C CAI	G CA' C GT H	AA T XTT A N	A CG A	G TT K	G ACA C TGT



Fig.24C.

		91			9				930			94	* •			50 *			960 *
AAG	CCG	CGG	GAG	GAG	CAG	TAC 2	AAC .	AGC	ACG	TAC	CGT	GTG	GTC	AGC	GTC	CTC	ACC	GTC .	CTG
MC	GGC	GCC	CTC	CTC	GTC	ATG '	TTG	TCG	TGC	ATG	GCA	CAC	CAG	TCG	CAG	GAG	TGG	CAG	GAC
K 301	P	R	E	E 305_	Q	Y	N	S hF	T CAC1	Y A _	R		V 	_315_	· V	<u></u>	T		.320>
JU4_								•					0						
			*			*			*				*			*			*
CAC	CAG	GAC	TGG	CTG	TAA	GGC .	AAG	GAG	TAC	AAG	TGC	AAG	GTC	TCC	AAC	AAA	GCC	CIC	CCA
GTG	GTC	CTG	ACC	GAC L	TTA N	CCG	IIC	CIC	AIG Y	K	ACG C	K	V	AGG S	N	K	A	L	P>
321_	<u>~</u>		· ••	_325_				}	τ C ΔC	1 A				_335_		····	· ·		_340>
		103	30		10	40		1	1050									:	1080
000	~~~	> m/2	*	AAA		* ~~~	₩ ~	תמת	*	ΔΔΔ			, *		GAA		CAG	GIG	* TAC
CGG	GGG	TAG	CTC	TTT	TGG	TAG	AGG	TTT	CGG	TTT	CCC	GTC	GGG	GCT	CIT	GGT	GTC	CAC	ATG
A	P	I	\mathbf{E}	K	${f T}$	I	S	K	A	K	G	Q	P	R ·	\mathbf{E}	P	Q.	V	Y>
341	<u></u>			_345_				n	الكلانا	- A _									_360>
		10	90 *		13	£00 ★		:	1110			11	20 *		1	130			1140 *
ACC	CIG	ccc	CCA	TCC	CGG	GAT	GAG	CTG	ACC	AAG	AAC	CAG	GTC	AGC	CIG	ACC	TGC	CIG	GIC
TGG	GAC	GGĢ	GGT	AGG	GCC	CTA	CIC	GAC	TGG	TTC	TTG	GTC	CAG	TCG	GAC	TGG	ACG	GAC	CAG V>
T 361	L	Р	P	s [.] 365	R	D	E	h	FCAC:	A LA_				ے _375		<u> </u>	<u>.</u>		_380>
•	•					•												,	1200
			*			*			*				*			*			*
AAA	GGC	TTC	TAT	CCC	AGC	GAC	ATC	GCC	GIG	GAG	ACC	CIC	AGC TCG	TTA	JUDU .	GIC	GGC	CIC	AAC TTG
K	G	F	Y	P	S	D	I	A	V	\mathbf{E}	W	E	S	N	G	Q	P	E	N>
381				_385				h	FCAC:	1 A .	<u></u>			_395		·			_400>
		12	210		1	220			1230			12			1	.250	,		1260
AAC	TAC	: AAG	ACC	ACG	CCT	ccc	GTG	CTG	GAC	TCC	GAC	GGC	TCC	TTC	TIC	CIC	TAC	AGC	AAG
TTC	ATC	TTC	TGG	TGC	GGA	GGG	CAC	GAC	CIG	AGG	CIG	CCC	AGC	AAC	AAC	GAG	ATC	TCC	TTC K>
N 401	Y	K	\mathbf{T}	т _405	P	P	V	L h	D FCAC	S 1 A	ם	G	<u>.</u>	۳ 415			Y	5	_420>
401		•											300			310			1320
			270 *			280			1290	•			*			*			*
CTC	ACC	GT	GAC	DAA C	AGC	AGG	TGG	CAG	CAG	GGG	AAC	GT	TTC	TCA	TGO	TCC	GTC	YFA :	G CAT
GA(TGC	CAC	CIG	TTC	TCG	TCC	ACC	CIV O	O GIO	. <i>CCC</i>	N TIG	CAL V	AAC F	انی A نو S	. ACC	S.	V.	M M	GTA H>
423	L			425	S			}}	1FCAC	1 A				_435	<u> </u>			, , , , , , , , , , , , , , , , , , , 	440>
		13	330		. 1	.340			1350)		13	360		:	1370			
				C AAC													מב ק	ነ ጥር	A
CTY	c cg	A GA	CGT	TTC	GTG	ATG	TGC	GTY	TIC	C TCC	GA(G AG	G GA	C AG	A GG		A TT	r ac	T
E	A	L	Н	N	H	Y	\mathbf{T}	Q	K	S	L	S	L	S	P	G	K	*	>
44	1	<u>-</u> _		_445	5	<u></u> — — —		hF(CAC1	A				45			458	ــــــــــــــــــــــــــــــــــــــ	_>

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Fig.25A.

DME - Challenge + Flt1D2VEGFR3D3.FcΔC1(a) + R→C + NAS + ΔB2 + A40 + Flt1 (1-3) Fc VEGF 165

Fig.25B.

DME - Challenge + Flt1D2VEGFR3D3.Fc Δ C1(a) + Flt1D2Flk1D3.Fc Δ C1(a) + R \rightarrow C + NAS + Δ B2 + A40 + Flt1 (1-3) Fc VEGF 165 DARFISH



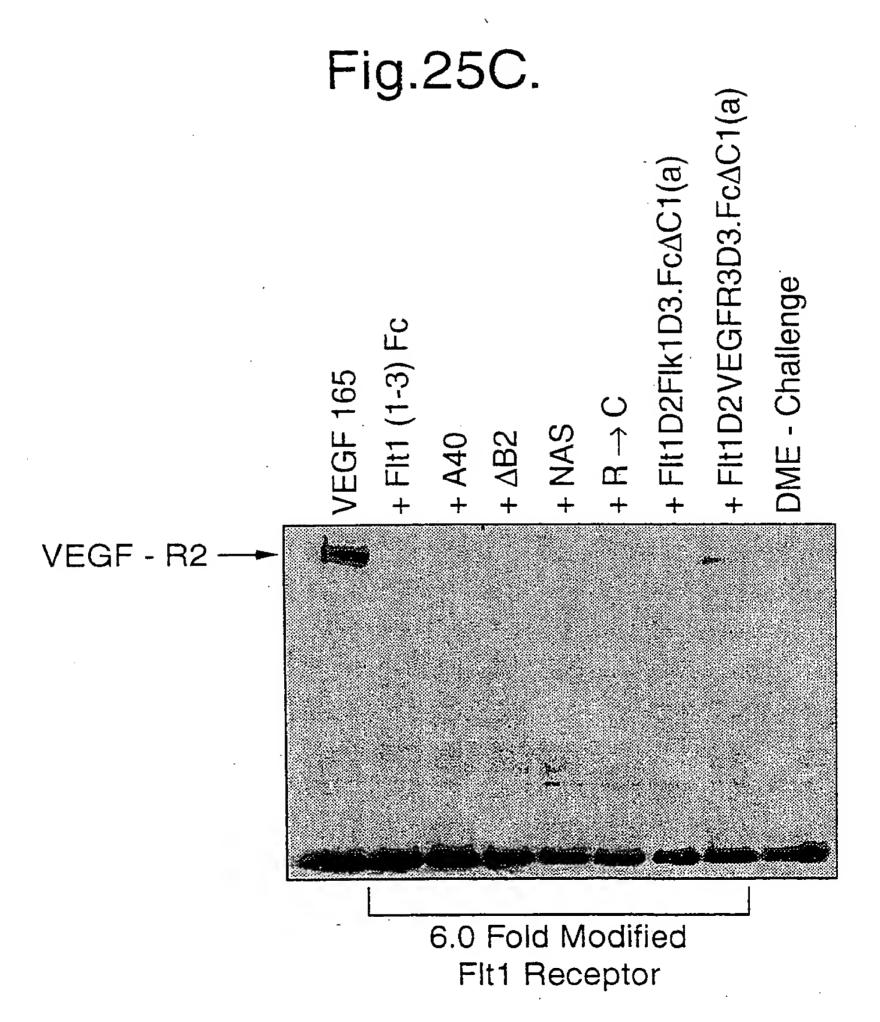




Fig.26A.

DME - Challenge tCHO-VEGFR1R2.FcΔC1(a) sCHO-Flt1D2Flk1D3.FcΔC1(a) tCHO-Flt1D2Flk1D3.FcΔC1(a) VEGF 165 tCHO-VEGFR1R2.FcΔC1(a) sCHO-Flt1D2Flk1D3.FcΔC1(a) tCHO-Flt1D2Flk1D3.FcΔC1(a)

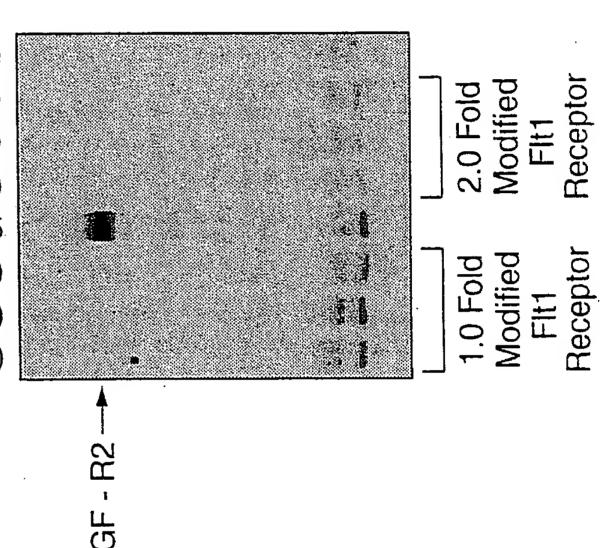
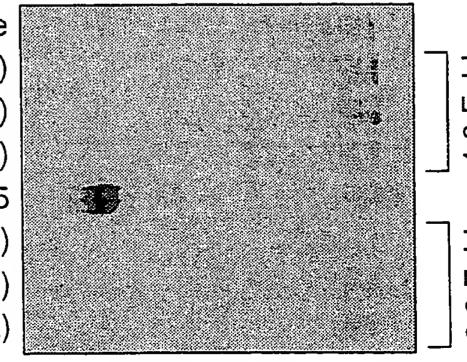


Fig.26B.

DME - Challenge tCHO-VEGFR1R2.FcΔC1(a) sCHO-Flt1D2Flk1D3.FcΔC1(a) tCHO-Flt1D2Flk1D3.FcΔC1(a) VEGF 165 tCHO-VEGFR1R2.FcΔC1(a) sCHO-Flt1D2Flk1D3.FcΔC1(a) tCHO-Flt1D2Flk1D3.FcΔC1(a)



- R2

VEGF

3.0 Fold 4.0 Fold Modified Flt1 Flt1 Receptor Receptor

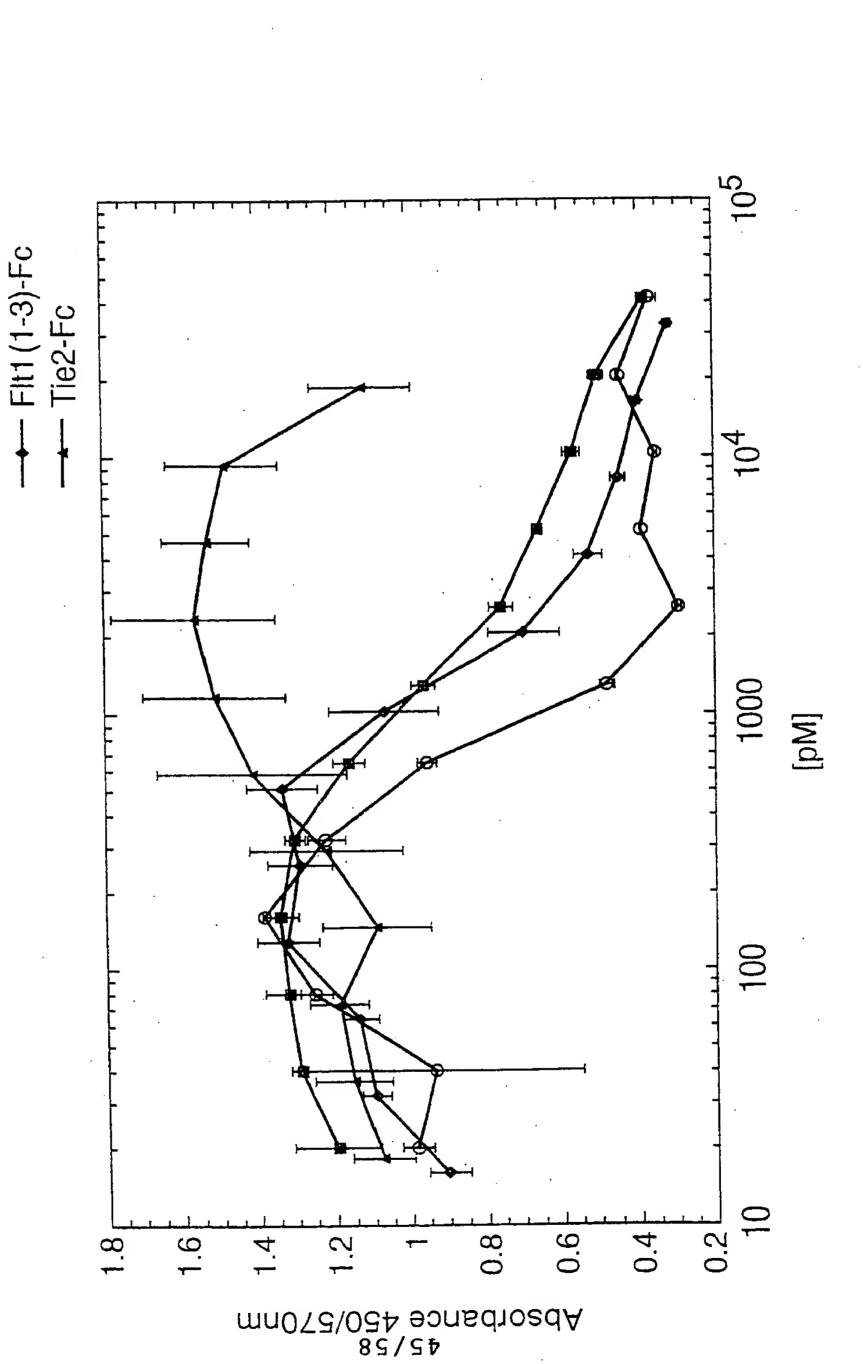
38 CHOCLASS

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Fig.27.

FIt1D2VEGFR3D3.FcdeltaC1(a)

FIt1D2Flk1D3.FcdeltaC1(a)





ORAFTSIA.

Fig. 28

	Binding St	Binding Stoichiometry of hVEGF165 to FIt1D2FIk1D3.	D2FIk1D3.FcΔC1(a) & VEGFR1R2-FcΔC1(a)
	hVEGF165 (nM)	VEGF/Flt1D2Flk1D3.FcΔC1(a)	VEGF/VEGFR1R2-FcΔC1(a)
89/	!	0.93	0.98
9₽	10	0.97	0.94
	50	•	0.99
	Average ± StDev	0.96 ± 0.03	0.97 ± 0.02

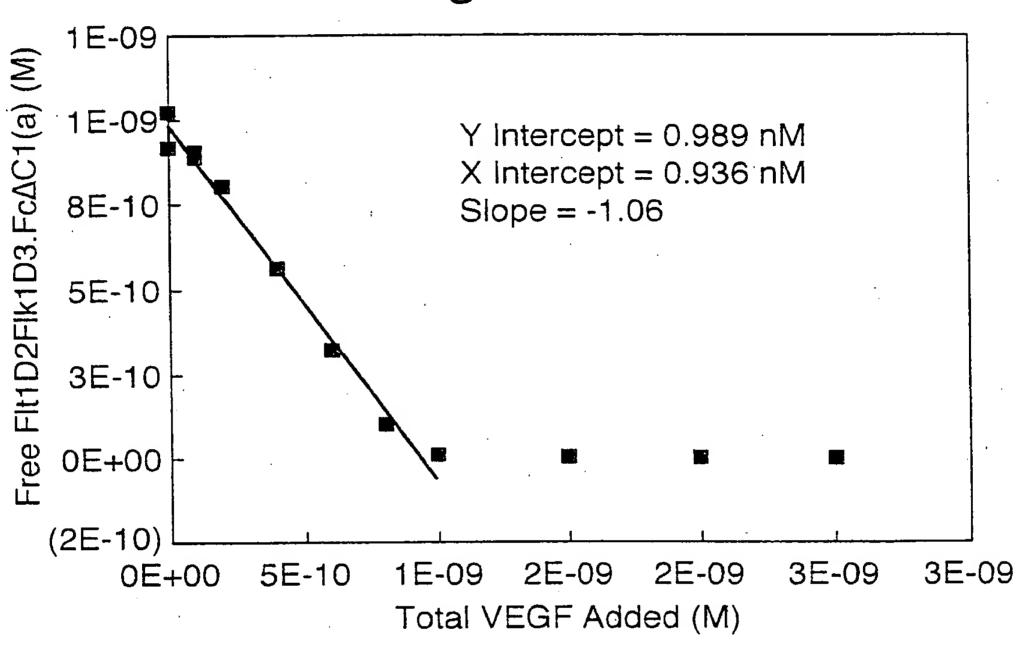


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Fig.29.



Slope = -1.07

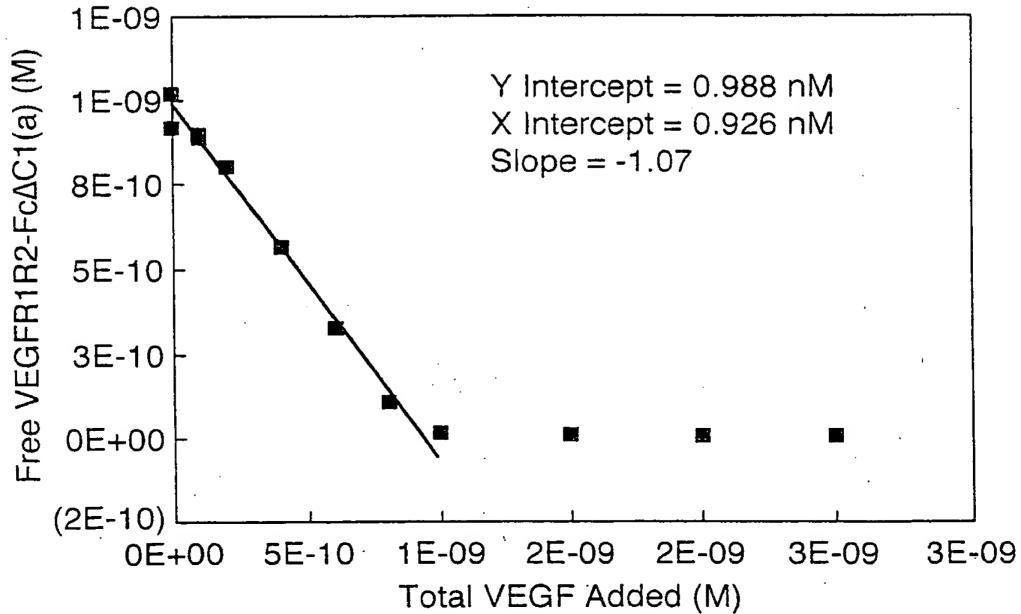
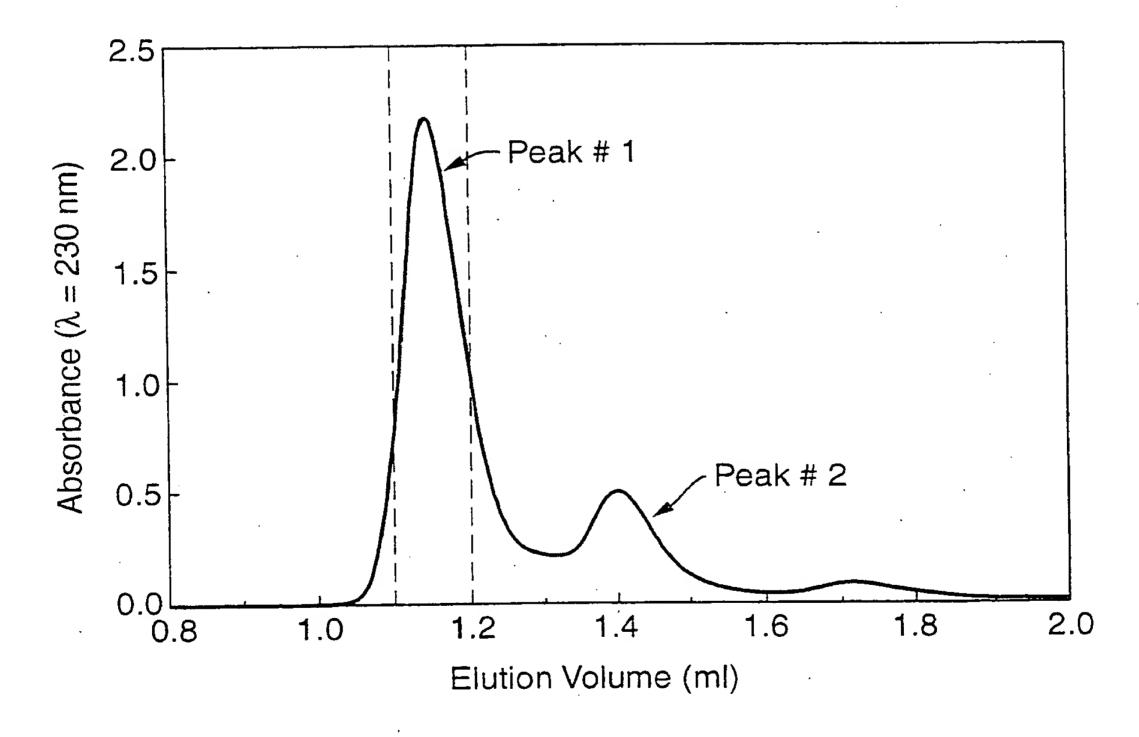
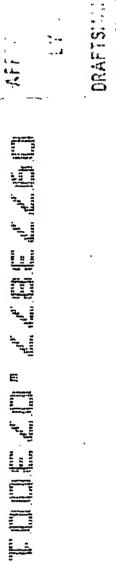


Fig.30.

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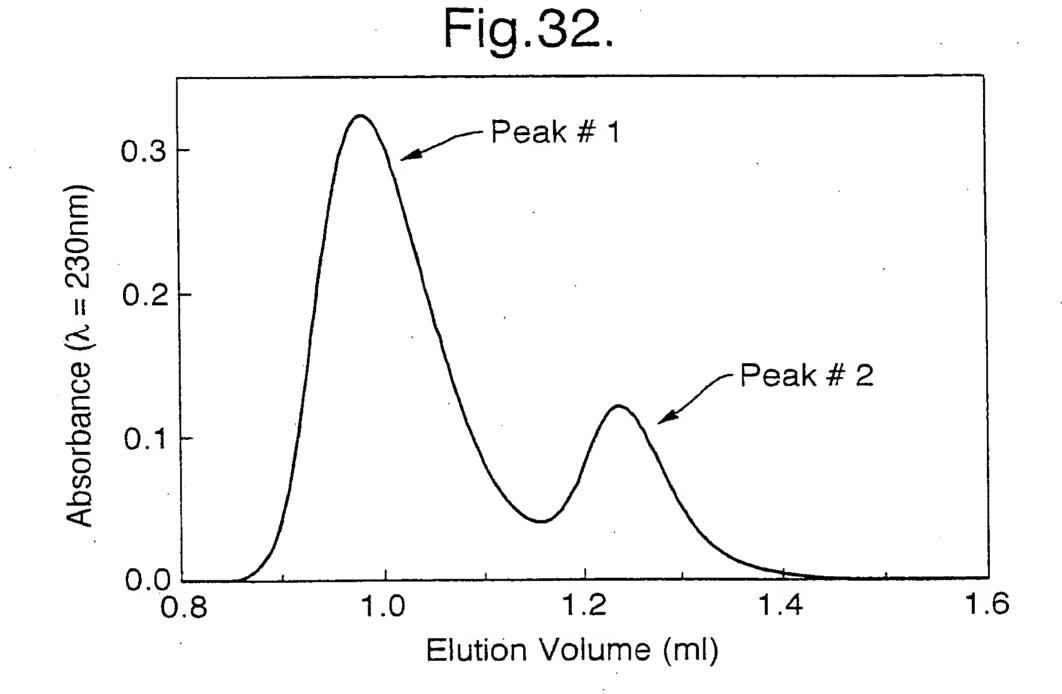
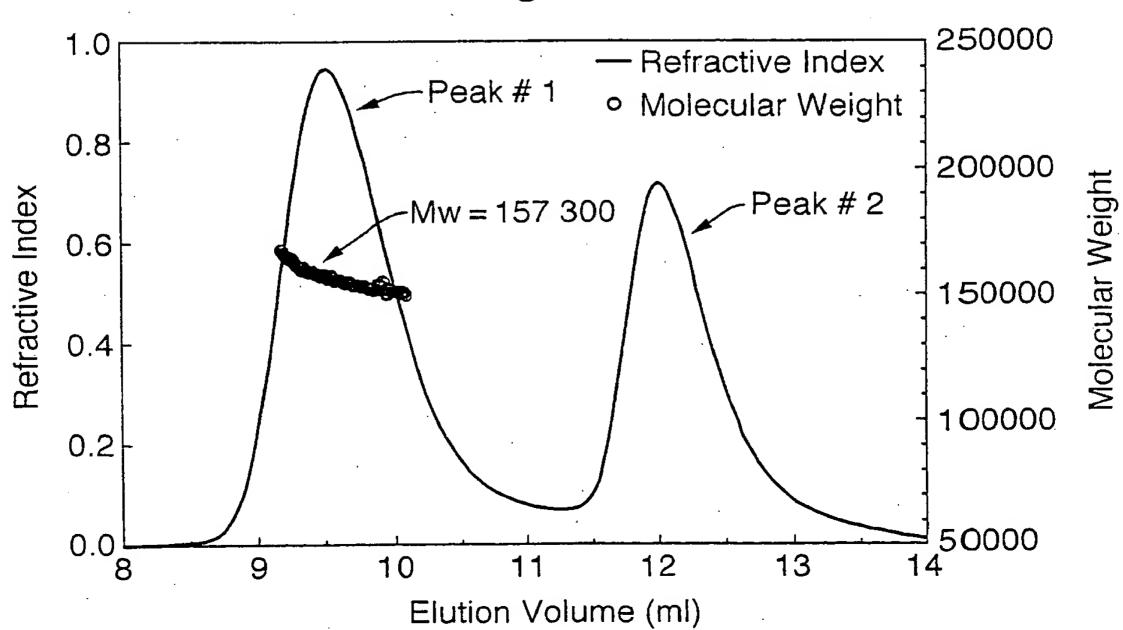
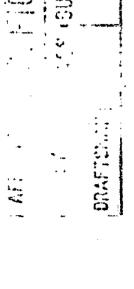
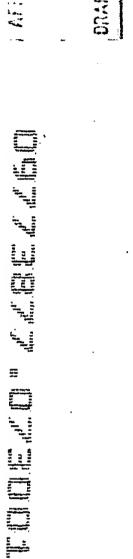
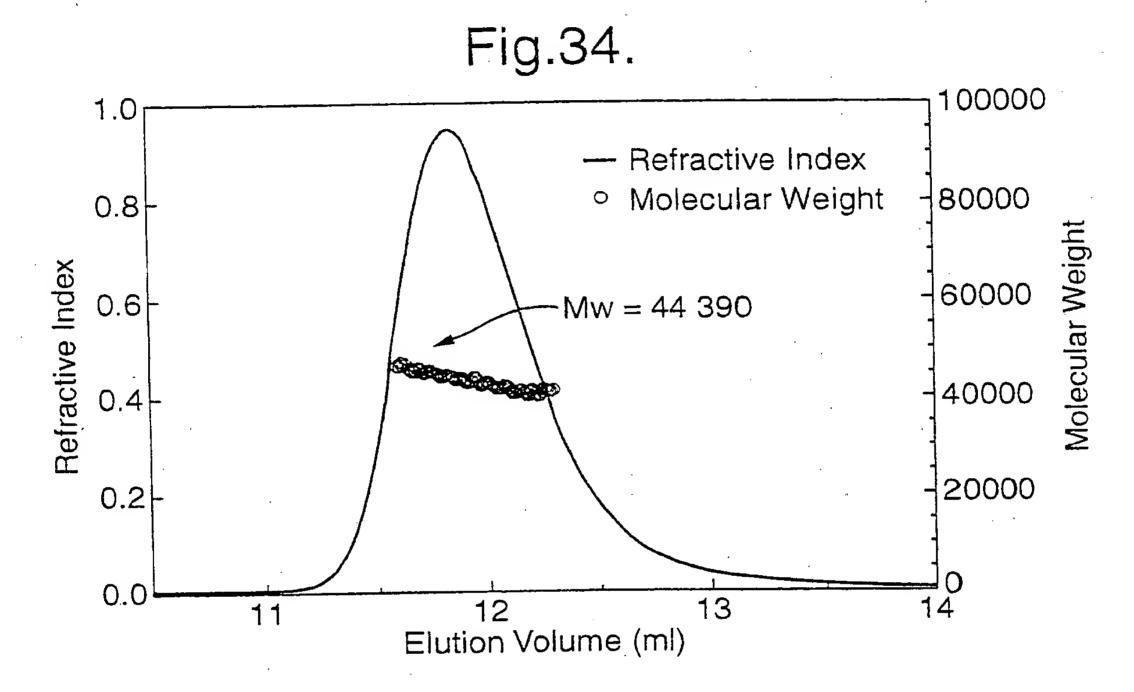


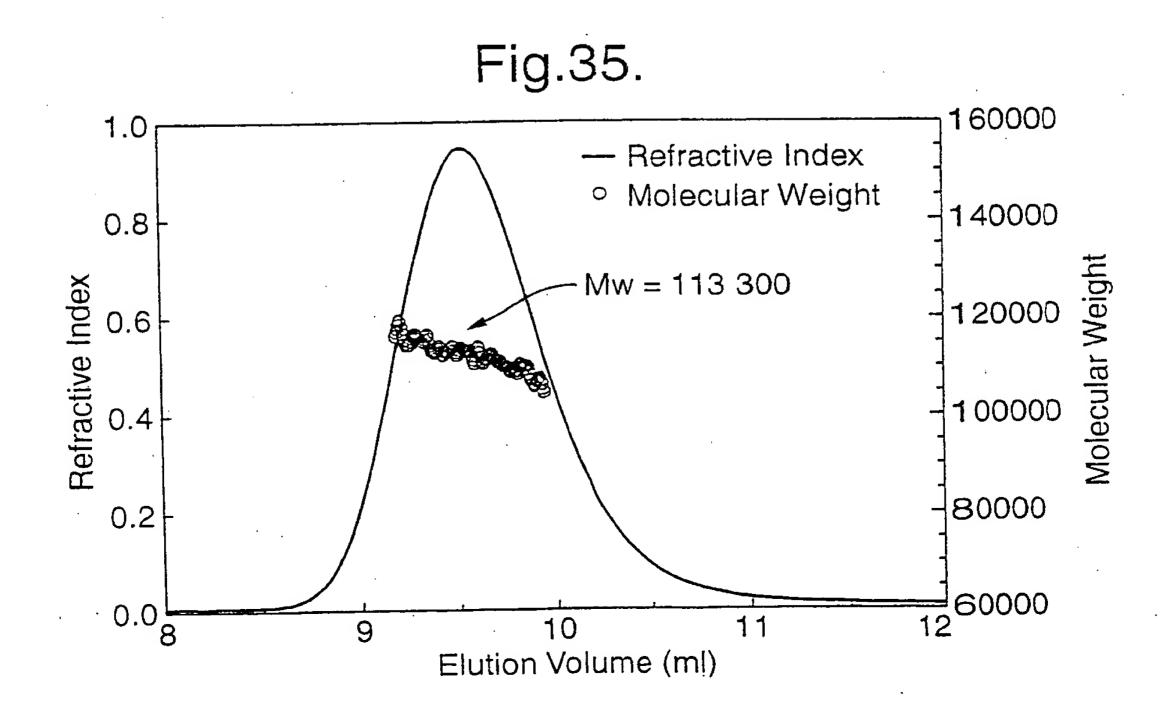
Fig.33.











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Fig.36.

VVI. SPSHGIEL SVGEKL VLNCTARTEL NVGIDFNWEYPSSKHQHKKL VNR KRIIWDSRKGFIIS<u>N</u>ATYKEIGLLT<u>C</u>EATVNGHLYKTNYLTHRQTNTIID GRPFVEMYSEIPEIIHMTEGRELVIPCRVTSP<u>N</u>ITVTLKKFPLDTLIPDG

DLKTQSGSEMKKFLSTLTIDGVTRSDQGLYTCAASSGLMTKKNSTFVRVH

350 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL

TCL VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL YSKL TVDKS

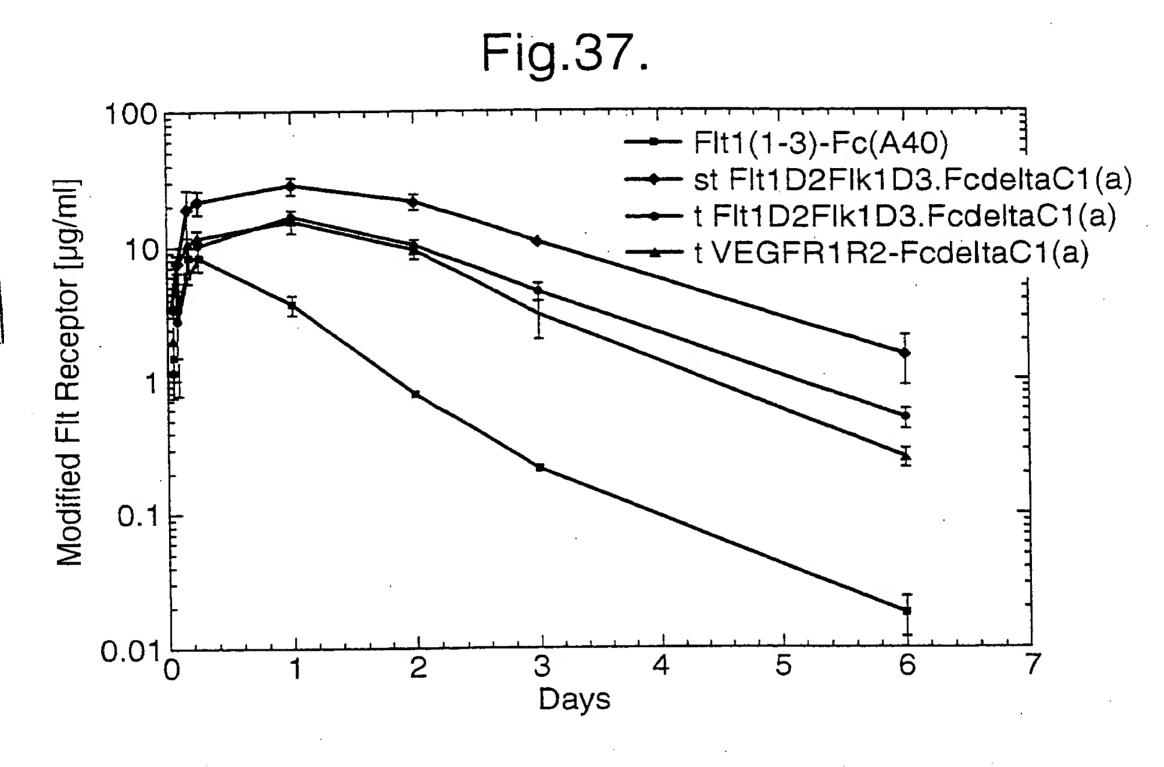
R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S P G K

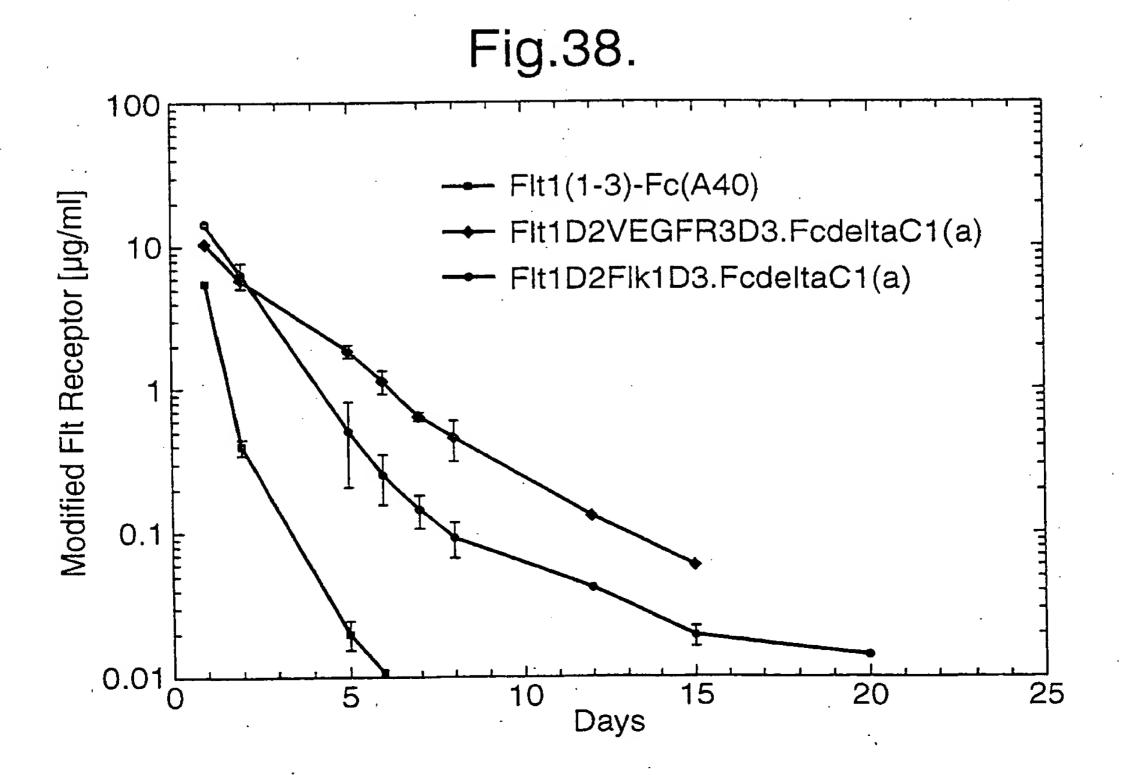




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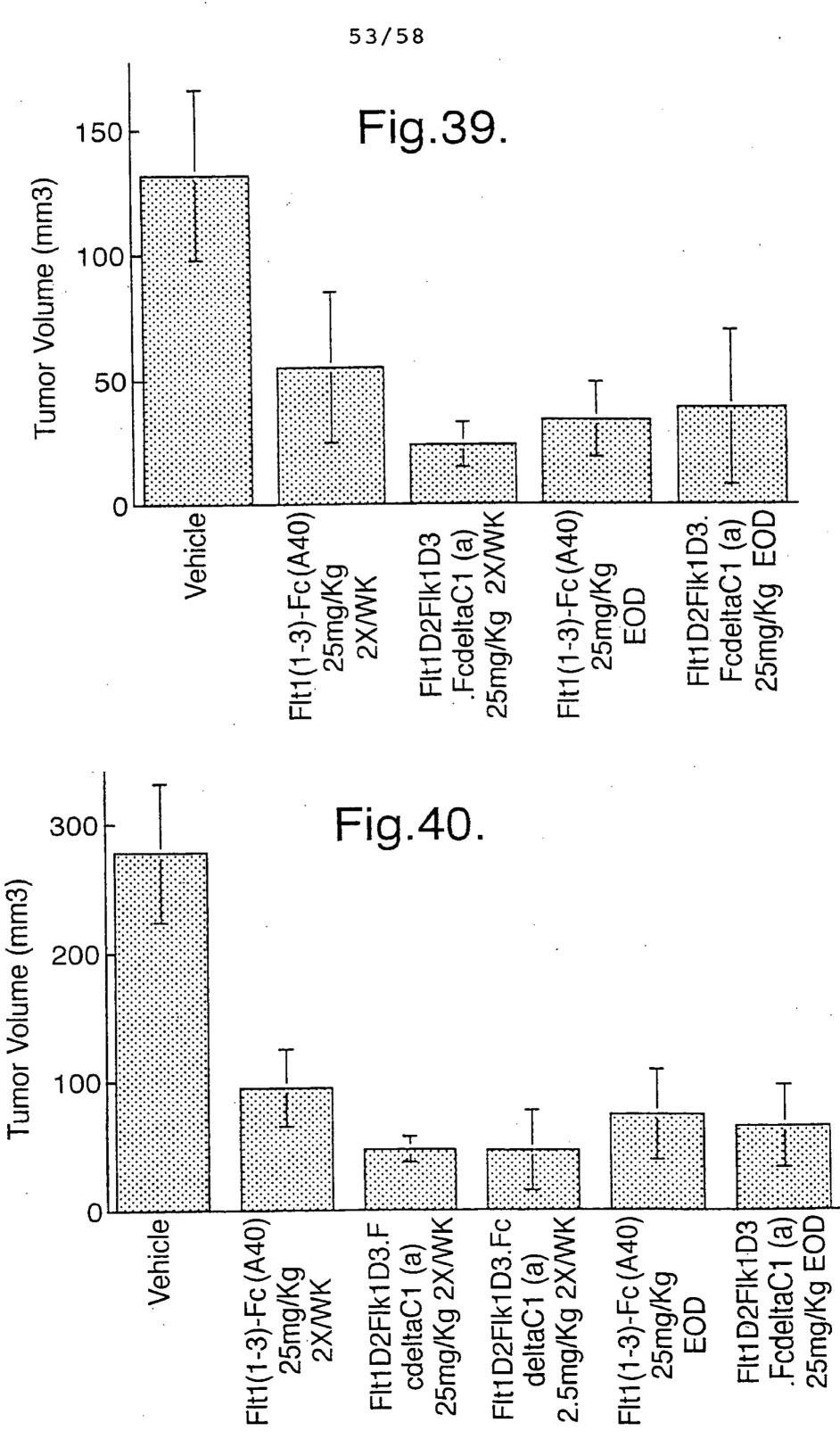




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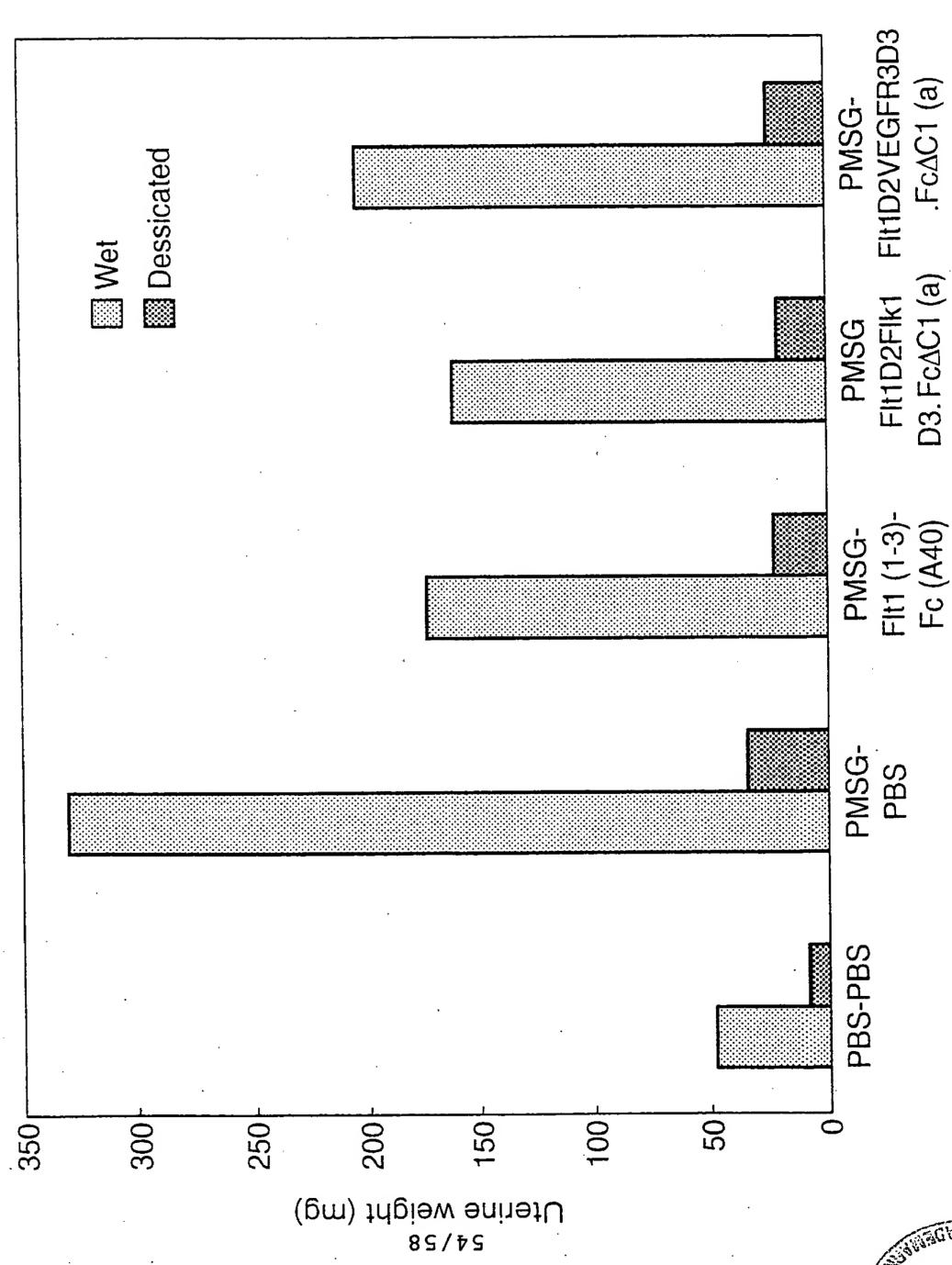
W.E.

The last the

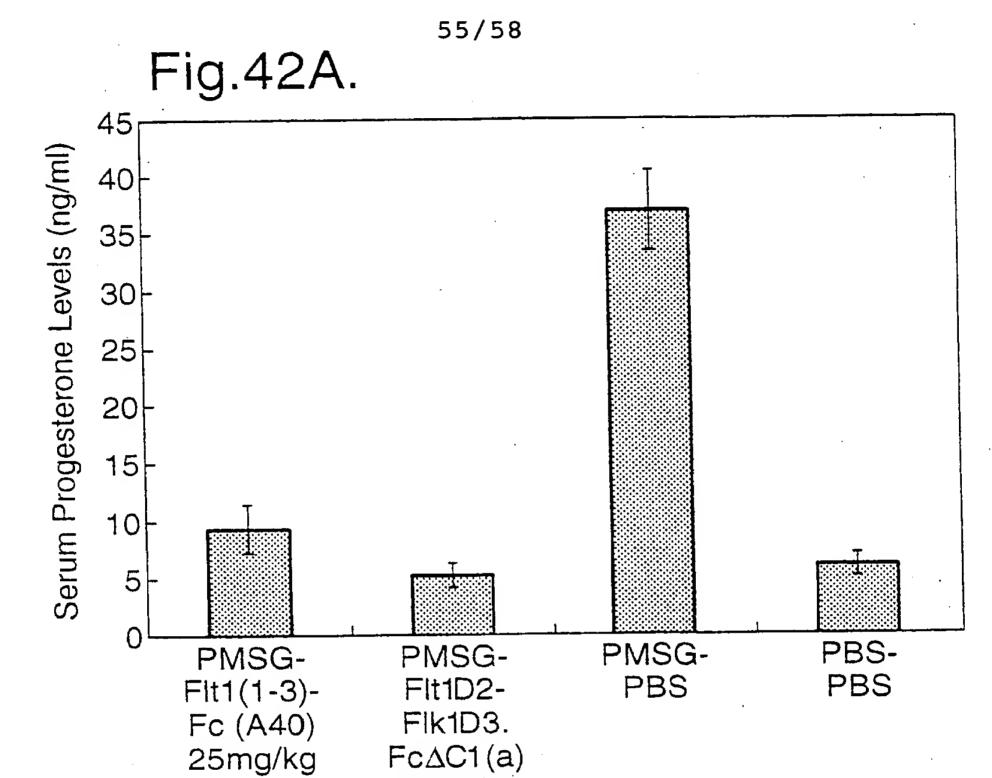


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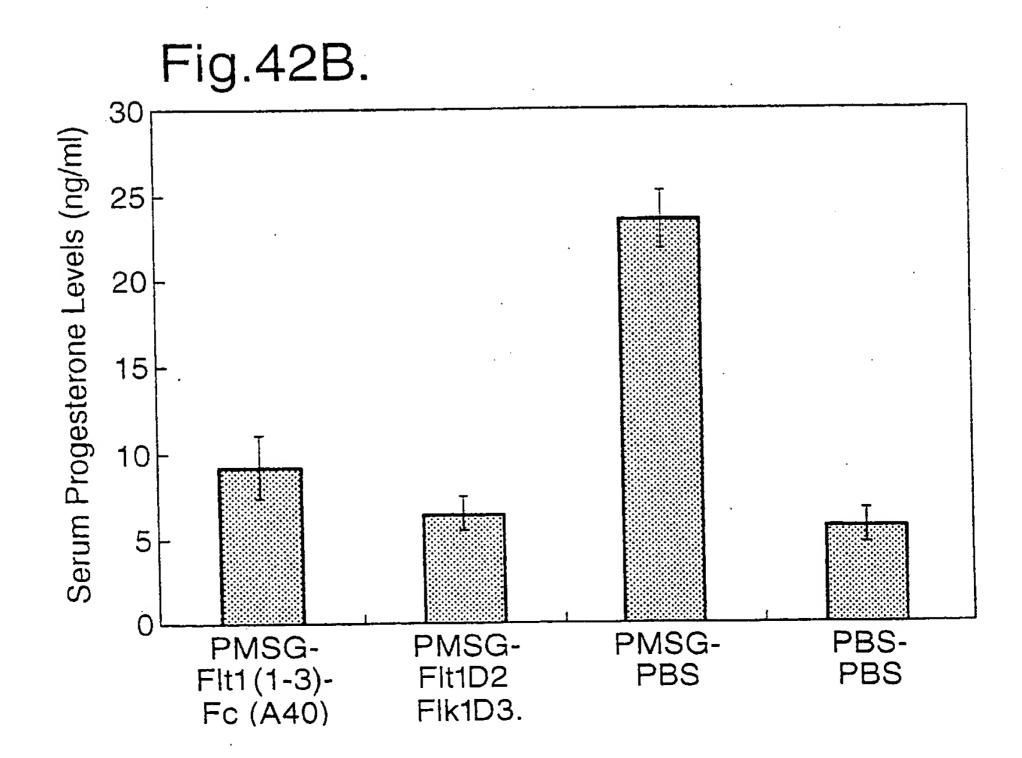
Fig. 41







25mg/kg

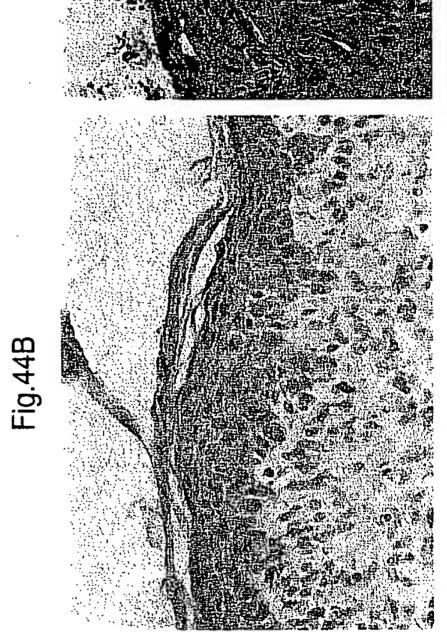


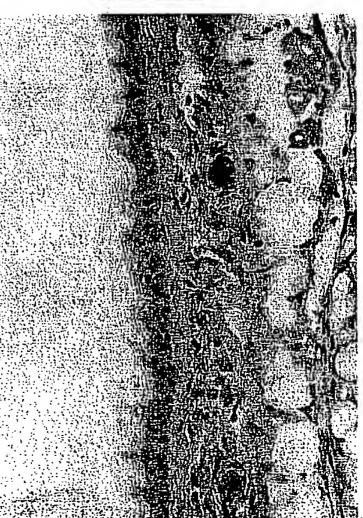
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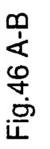
Fig.44 A-C

Fig.44C













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Fig47G Fig470 Fig47K Fig47C Fig47E



